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  (FILE 'HOME' ENTERED AT 15:21:29 ON 08 OCT 2003)

     FILE 'REGISTRY' ENTERED AT 15:24:35 ON 08 OCT 2003
L1             1 S EZETIMIBE/CN
L2             1 S CHOLESTYRAMINE/CN
L3             1 S SIMVASTATIN/CN

     FILE 'CAPLUS, USPATFULL, EMBASE, MEDLINE, BIOSIS' ENTERED AT 15:29:26 ON
     08 OCT 2003
L4           593 S EZETIMIBE OR 163222-33-1/RN
L5         14728 S SIMVASTATIN OR 79902-63-9/RN
L6         10124 S CHOLESTYRAMINE OR 11041-12-6/RN
L7            25 S L4 AND SITOSTEROLEMIA
L8            21 DUP REM L7 (4 DUPLICATES REMOVED)
L9            24 S L5 AND SITOSTEROLEMIA
L10           19 DUP REM L9 (5 DUPLICATES REMOVED)
L11           56 S L6 AND SITOSTEROLEMIA
L12           15 S L11 AND L10
L13           15 DUP REM L12 (0 DUPLICATES REMOVED)

=> s l4 and l5 and l6 and sitosterolemia
L14           14 L4 AND L5 AND L6 AND SITOSTEROLEMIA

=> dup rem l14
PROCESSING COMPLETED FOR L14
L15           14 DUP REM L14 (0 DUPLICATES REMOVED)

=> d l15 1-14 ab bib kwic

L15  ANSWER 1 OF 14  USPATFULL on STN
AB      The present invention provides therapeutic combinations and methods
        including at least one sterol or 5.alpha.-stanol absorption inhibitor
        that can be useful for treating xanthomas.
AN      2003:173961  USPATFULL
TI      Methods and therapeutic combinations for the treatment of xanthoma using
        sterol absorption inhibitors
IN      Davis, Harry R., Berkeley Heights, NJ, UNITED STATES
PA      Schering Corporation (U.S. corporation)
PI      US 2003119809      A1   20030626
AI      US 2002-247095     A1   20020919 (10)
PRAI    US 2001-323942P     20010921 (60)
DT      Utility
FS      APPLICATION
LREP    SCHERING-PLOUGH CORPORATION, PATENT DEPARTMENT (K-6-1, 1990), 2000
        GALLOPING HILL ROAD, KENILWORTH, NJ, 07033-0530
CLMN    Number of Claims: 23
ECL     Exemplary Claim: 1
DRWN    No Drawings
LN.CNT 2722
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
SUMM    . . . of Formula (I) useful in the compositions, therapeutic
        combinations and methods of the present invention is represented by
        Formula (II) (ezetimibe) below:   ##STR2##
SUMM    . . . MEVACOR.RTM. which is available from Merck & Co.), pravastatin
        (for example PRAVACHOL.RTM. which is available from Bristol Meyers
        Squibb), fluvastatin, simvastatin (for example ZOCOR.RTM.
        which is available from Merck & Co.), atorvastatin, cerivastatin,
        CI-981, rivastatin (sodium 7-(4-fluorophenyl)-2,6-diisopropyl-5-
        methoxymethylpyridin-3-yl )-3,5-dihydroxy-6-heptanoate), rosuvastatin
        and pitavastatin. . . NB-598 ((E)-N-ethyl-N-(6,6-dimethyl-2-hepten-4-
        ynyl)-3-[(3,3'-bithiophen-5-yl)methoxy]benzene-methanamine
        hydrochloride) and other sterol biosynthesis inhibitors such as DMP-565.
        Preferred HMG CoA reductase inhibitors include lovastatin, pravastatin
        and simvastatin. The most preferred HMG CoA reductase
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inhibitor is **simvastatin**.

SUMM [0380] Non-limiting examples of suitable bile acid sequestrants include **cholestyramine** (a styrene-divinylbenzene copolymer containing quaternary ammonium cationic groups capable of binding bile acids, such as QUESTRAN.RTM. or QUESTRAN LIGHT.RTM. **cholestyramine** which are available from Bristol-Myers Squibb), colestipol (a copolymer of diethylenetriamine and 1-chloro-2,3-epoxypropane, such as COLESTID.RTM. tablets which are available. . .

DETD . . . cholesterol in mammals, and can be useful in the treatment and/or prevention of vascular conditions, such as atherosclerosis, hypercholesterolemia and **sitosterolemia**, vascular inflammation, stroke, obesity and lowering of plasma levels of cholesterol in subjects, in particular in humans. As used herein,. . .

CLM What is claimed is:

. . . The method according to claim 13, wherein the HMG-CoA reductase inhibitor is selected from the group consisting of pravastatin, lovastatin, **simvastatin**, fluvastatin, rivastatin, rosuvastatin, atorvastatin, cerivastatin, and combinations thereof.

IT **163222-33-1P**
(sterol/5.alpha.-stanol absorption inhibitors for treatment of xanthoma, and use with other agents)

IT 59-67-6, Nicotinic acid, biological studies 59-67-6D, Nicotinic acid, derivs. 23288-49-5, Probucol 23288-49-5D, Probucol, derivs. 55121-56-7D, Azetidinone, derivs. 75330-75-5, Lovastatin **79902-63-9**, Simvastatin 81093-37-0, Pravastatin 93957-54-1, Fluvastatin 134523-00-5, Atorvastatin 143201-11-0, Rivastatin 145599-86-6, Cerivastatin 287714-41-4, Rosuvastatin
(sterol/5.alpha.-stanol absorption inhibitors for treatment of xanthoma, and use with other agents)

L15 ANSWER 2 OF 14 USPATFULL on STN

AB The present invention relates to methods of treating or preventing cardiovascular conditions while preventing or minimizing muscular degeneration side effects associated with certain HMG-CoA reductase inhibitors by coadministration of at least one sterol or 5.alpha.-stanol absorption inhibitor, pharmaceutically acceptable salts or solvates thereof, and at least one HMG-CoA reductase inhibitor, the latter being used sparingly in amounts insufficient to cause muscle degeneration.

AN 2003:173960 USPATFULL

TI Methods of treating or preventing cardiovascular conditions while preventing or minimizing muscular degeneration side effects

IN LeBeaut, Alexandre P., Morristown, NJ, UNITED STATES
Davis, Harry R., Berkeley Heights, NJ, UNITED STATES

PA Schering Corporation (U.S. corporation)

PI US 2003119808 A1 20030626

AI US 2002-246996 A1 20020919 (10)

PRAI US 2001-324121P 20010921 (60)
US 2002-351957P 20020125 (60)

DT Utility

FS APPLICATION

LREP SCHERING-PLOUGH CORPORATION, PATENT DEPARTMENT (K-6-1, 1990), 2000 GALLOPING HILL ROAD, KENILWORTH, NJ, 07033-0530

CLMN Number of Claims: 23

ECL Exemplary Claim: 1

DRWN No Drawings

LN.CNT 3092

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

SUMM . . . MEVACOR.RTM. which is available from Merck & Co.), pravastatin (for example PRAVACHOL.RTM. which is available from Bristol Meyers Squibb), fluvastatin, **simvastatin** (for example ZOCOR.RTM. which is available from Merck & Co.), atorvastatin, [cerivastatin] withdrawn from the market, CI-981, rivastatin (sodium 7-(4-fluorophenyl)-2,6-diisopropyl-5-methoxymethylpyridin-3-yl)-3,5-

dihydroxy-6-heptanoate). . . pitavastatin (such as NK-104 of Negma Kowa of Japan). Preferred HMG CoA reductase inhibitors include lovastatin, pravastatin , atorvastatin and **simvastatin**. The most preferred HMG CoA reductase inhibitors are **simvastatin** and atorvastatin.

SUMM . . . with the at least one sterol or 5.alpha.-stanol absorption inhibitor, e.g.;

HMG CoA Reductase Inhibitor	Approved Dose (mg)
simvastatin	5, 10, 20, 40, 80
pravastatin	10, 20, 40
atorvastatin	10, 20, 40, 80
lovastatin	10, 20, 40

SUMM . . . of Formula (I) useful in the compositions, therapeutic combinations and methods of the present invention is represented by Formula (II) (**ezetimibe**) below: ##STR2##

SUMM [0393] Non-limiting examples of suitable bile acid sequestrants include **cholestyramine** (a styrene-divinylbenzene copolymer containing quaternary ammonium cationic groups capable of binding bile acids, such as QUESTRAN.RTM. or QUESTRAN LIGHT.RTM. **cholestyramine** which are available from Bristol-Myers Squibb), colestipol (a copolymer of diethylenetriamine and 1-chloro-2,3-epoxypropane, such as COLESTID.RTM. tablets which are available. . .

SUMM . . . can further be used to treat or prevent vascular disease or conditions (such as for example atherosclerosis, arteriosclerosis, hypercholesterolemia and/or **sitosterolemia**), cardiovascular events, hypertension, obesity, stroke, lowering of a concentration of a sterol in plasma of a mammal, reducing vascular inflammation. . .

SUMM . . . the above-described tablet can be coadministered with a tablet, capsule, etc. comprising a dosage of Active Compound II, for example **simvastatin** as described above.

SUMM . . . 5.alpha.-stanols in subjects and can be useful in the treatment and/or prevention of vascular conditions, such as atherosclerosis, hypercholesterolemia and **sitosterolemia**, stroke, obesity and lowering of plasma levels of sterols such as cholesterol or 5.alpha.-stanols in subject, in particular in humans.

CLM What is claimed is:

. . . 1, wherein the at least one HMG-CoA reductase inhibitor is selected from the group consisting of lovastatin, pravastatin, rivastatin, fluvastatin, **simvastatin**, atorvastatin, cerivastatin and combinations thereof.

15. The method of claim 1, wherein the at least one HMG-CoA reductase inhibitor is **simvastatin**.

IT 75330-75-5, Lovastatin **79902-63-9**, Simvastatin 81093-37-0, Pravastatin 93957-54-1, Fluvastatin 134523-00-5, Atorvastatin 143201-11-0, Rivastatin 145599-86-6, Cerivastatin
(HMG-CoA reductase inhibitor; sterol or 5.alpha.-stanol absorption inhibitor and HMG-CoA reductase inhibitor for treating or preventing cardiovascular conditions while preventing muscle degeneration side effects)

IT **163222-33-1P**, Ezetimibe
(sterol or 5.alpha.-stanol absorption inhibitor; sterol or 5.alpha.-stanol absorption inhibitor and HMG-CoA reductase inhibitor for treating or preventing cardiovascular conditions while preventing muscle degeneration side effects)

L15 ANSWER 3 OF 14 USPATFULL on STN

AB The present invention provides compositions, therapeutic combinations and methods including: (a) at least one hormone replacement therapy composition; and (b) at least one sterol absorption inhibitor which can

be useful for treating vascular conditions in post-menopausal women and lowering plasma levels of sterols or 5.alpha.-stanols.

AN 2003:173948 USPATFULL

TI Combinations of hormone replacement therapy composition(s) and sterol absorption inhibitor(s) and treatments for vascular conditions in post-menopausal women

IN Strony, John T., Lebanon, NJ, UNITED STATES

PA Schering Corporation (U.S. corporation)

PI US 2003119796 A1 20030626

AI US 2002-247085 A1 20020919 (10)

RLI Continuation-in-part of Ser. No. US 2002-166942, filed on 11 Jun 2002, PENDING

PRAI US 2001-324118P 20010921 (60)

DT Utility

FS APPLICATION

LREP SCHERING-PLOUGH CORPORATION, PATENT DEPARTMENT (K-6-1, 1990), 2000 GALLOPING HILL ROAD, KENILWORTH, NJ, 07033-0530

CLMN Number of Claims: 44

ECL Exemplary Claim: 1

DRWN No Drawings

LN.CNT 2932

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

SUMM . . . or halting of progression of the condition, for example a vascular condition, such as hyperlipidaemia (for example atherosclerosis, hypercholesterolemia or **sitosterolemia**), vascular inflammation, stroke, diabetes, obesity and/or reduce the level of sterol(s) (such as cholesterol) in the plasma of a patient,. . .

SUMM . . . of Formula (I) useful in the compositions, therapeutic combinations and methods of the present invention is represented by Formula (II) (**ezetimibe**) below: ##STR2##

SUMM . . . MEVACOR.RTM. which is available from Merck & Co.), pravastatin (for example PRAVACHOL.RTM. which is available from Bristol Meyers Squibb), fluvastatin, **simvastatin** (for example ZOCOR.RTM. which is available from Merck & Co.), atorvastatin, cerivastatin, CI-981, rivastatin (sodium 7-(4-fluorophenyl)-2,6-diisopropyl-5-methoxymethylpyridin-3-yl)-3,5-dihydroxy-6-heptanoate) and pitavastatin (such as. . . NB-598 ((E)-N-ethyl-N-(6,6-dimethyl-2-hepten-4-ynyl)-3-[(3,3'-bithiophen-5-yl)methoxy]benzene-methanamine hydrochloride) and other sterol biosynthesis inhibitors such as DMP-565. Preferred HMG CoA reductase inhibitors include lovastatin, pravastatin and **simvastatin**. The most preferred HMG CoA reductase inhibitor is **simvastatin**.

SUMM [0406] Non-limiting examples of suitable bile acid sequestrants include **cholestyramine** (a styrene-divinylbenzene copolymer containing quaternary ammonium cationic groups capable of binding bile acids, such as QUESTRAN.RTM. or QUESTRAN LIGHT.RTM. **cholestyramine** which are available from Bristol-Myers Squibb), colestipol (a copolymer of diethylenetriamine and 1-chloro-2,3-epoxypropane, such as COLESTID.RTM. tablets which are available. . .

DETD . . . 5.alpha.-stanol in subjects and can be useful in the treatment and/or prevention of vascular conditions, such as atherosclerosis, hypercholesterolemia and **sitosterolemia**, stroke, obesity and lowering of plasma levels of cholesterol in mammals, in particular in humans such as women, and preferably. . .

CLM What is claimed is:

. . . 22, wherein the at least one HMG CoA reductase inhibitor is selected from the group consisting of lovastatin, pravastatin, fluvastatin, **simvastatin**, atorvastatin, cerivastatin and mixtures thereof.

24. The composition according to claim 23, wherein the at least one HMG CoA reductase inhibitor is **simvastatin**.

IT 50-28-2, Estradiol, biological studies 57-63-6, Ethinyl estradiol 57-83-0, Pregn-4-ene-3, 20-dione, biological studies 58-18-4,

Methyltestosterone 59-67-6, Nicotinic acid, biological studies 68-22-4, Norethindrone 71-58-9, Medroxyprogesterone acetate 72-33-3, Mestranol 297-76-7, Ethynodiol diacetate 438-67-5, Sodium estrone sulfate 520-85-4, Medroxyprogesterone 797-63-7, Levonorgestrel 4999-79-5, 17.beta.-Estradiol sodium sulfate 6533-00-2, Norgestrel 16680-47-0, Sodium equilin sulfate 16680-48-1, Equilenin sodium sulfate 16680-49-2, Sodium 17.beta.-dihydroequilin sulfate 16680-50-5, 17.beta.-Dihydroequilenin sodium sulfate 23288-49-5, Probucol 35189-28-7, Norgestimate 38600-07-6, Sodium 17.alpha.-estradiol sulfate 38600-08-7, Sodium 17.alpha.-dihydroequilenin sulfate 38600-09-8, Sodium 17.alpha.-dihydroequilin sulfate 54024-22-5, Desogestrel 75330-75-5, Lovastatin **79902-63-9**, Simvastatin 81093-37-0, Pravastatin 93957-54-1, Fluvastatin 134523-00-5, Atorvastatin 145599-86-6, Cerivastatin
(combinations of hormone replacement therapy compn.(s) and sterol absorption inhibitor(s) and treatments for vascular conditions in post-menopausal women)

IT 163222-32-0P **163222-33-1P** 163380-15-2P
(synthesis of sterol absorption inhibitors for the combined use with hormone replacement therapy compns. and treatments for vascular conditions in post-menopausal women)

L15 ANSWER 4 OF 14 USPATFULL on STN

AB The present invention provides methods for treating or preventing vascular inflammation or for reducing blood levels of c-reactive protein by administering at least one sterol absorption inhibitor and/or at least one 5.alpha.-stanol absorption inhibitor.

AN 2003:173909 USPATFULL

TI Methods for treating or preventing vascular inflammation using sterol absorption inhibitor(s)

IN Davis, Harry R., Berkeley Heights, NJ, UNITED STATES

PA Schering Corporation (U.S. corporation)

PI US 2003119757 A1 20030626

AI US 2002-247032 A1 20020919 (10)

RLI Continuation-in-part of Ser. No. US 2002-166942, filed on 11 Jun 2002, PENDING

PRAI US 2001-323937P 20010921 (60)

DT Utility

FS APPLICATION

LREP SCHERING-PLOUGH CORPORATION, PATENT DEPARTMENT (K-6-1, 1990), 2000 GALLOPING HILL ROAD, KENILWORTH, NJ, 07033-0530

CLMN Number of Claims: 35

ECL Exemplary Claim: 1

DRWN No Drawings

LN.CNT 3032

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

SUMM . . . of Formula (I) useful in the compositions, therapeutic combinations and methods of the present invention is represented by Formula (II) (**ezetimibe**) below: ##STR3##

SUMM . . . MEVACOR.RTM. which is available from Merck & Co.), pravastatin (for example PRAVACHOL.RTM. which is available from Bristol Meyers Squibb), fluvastatin, **simvastatin** (for example ZOCOR.RTM. which is available from Merck & Co.), atorvastatin, cerivastatin, CI-981 and pitavastatin (such as NK-104 of Negma. . . NB-598 ((E)-N-ethyl-N-(6,6-dimethyl-2-hepten-4-ynyl)-3-[(3,3'-bithiophen-5-yl)methoxy]benzene-methanamine hydrochloride) and other sterol biosynthesis inhibitors such as DMP-565. Preferred HMG CoA reductase inhibitors include lovastatin, pravastatin and **simvastatin**. The most preferred HMG CoA reductase inhibitor is **simvastatin**.

SUMM . . . Preferably the cholesterol biosynthesis inhibitor comprises one or more HMG CoA reductase inhibitors, such as, for example, lovastatin, pravastatin and/or **simvastatin**. More preferably, the method comprises the compound of Formula (II) in combination with **simvastatin** and gemfibrozil or fenofibrate.

SUMM [0405] Non-limiting examples of suitable bile acid sequestrants include **cholestyramine** (a styrene-divinylbenzene copolymer containing quaternary ammonium cationic groups capable of binding bile acids, such as QUESTRAN.RTM. or QUESTRAN LIGHT.RTM. **cholestyramine** which are available from Bristol-Myers Squibb), colestipol (a copolymer of diethylenetriamine and 1-chloro-2,3-epoxypropane, such as COLESTID.RTM. tablets which are available. . .

DETD . . . blood and can be useful in the treatment as well as prevention of vascular conditions, such as atherosclerosis, hypercholesterolemia and **sitosterolemia**, stroke, obesity and lower plasma levels of sterols and/or 5.alpha.-stanols in a subject, in particular in humans, such as phytosterols. . .

DETD . . . 12 consecutive weeks: a tablet formulation as described above having 10 milligrams of the compound of Formula (II) "Composition A"; **SIMVASTATIN** 10, 20, 40 or 80 mg (available from Merck & Co., Inc.); coadministration of Composition A+**SIMVASTATIN** 10, 20, 40 or 80 mg; or placebo.

DETD [0512] Pooled subjects treated with Composition A+**SIMVASTATIN** had reduced LDL-C from baseline by 49.9% vs. pooled subjects treated with **SIMVASTATIN** alone (36.1%, P<0.01) and co-administration of Composition A+**SIMVASTATIN** was superior to statin alone at each **SIMVASTATIN** dose. Overall, median percent reductions in CRP from baseline were almost 2.times.greater with pooled Composition A+ **SIMVASTATIN** vs. pooled **SIMVASTATIN** alone (-34.8% vs -18.2%, P<0.01). Median CRP was reduced in pooled Composition A+ **SIMVASTATIN** to 0.180 mg/dL and with **SIMVASTATIN** to 0.215 mg/dL (P=0.03). CRP reductions by Composition A+ **SIMVASTATIN** were comparable to **SIMVASTATIN** 80.

CLM What is claimed is:

. . . 19, wherein the at least one HMG CoA reductase inhibitor is selected from the group consisting of lovastatin, pravastatin, fluvastatin, **simvastatin**, atorvastatin, cerivastatin and mixtures thereof.

IT 75330-75-5, Lovastatin **79902-63-9**, Simvastatin 81093-37-0, Pravastatin 93957-54-1, Fluvastatin 134523-00-5, Atorvastatin 145599-86-6, Cerivastatin
(HMG-CoA reductase inhibitor; sterol or 5.alpha.-stanol absorption inhibitor for reducing blood levels of C-reactive protein and treating or preventing vascular inflammation)

IT **163222-33-1P**, Ezetimibe
(sterol or 5.alpha.-stanol absorption inhibitor; sterol or 5.alpha.-stanol absorption inhibitor for reducing blood levels of C-reactive protein and treating or preventing vascular inflammation)

L15 ANSWER 5 OF 14 USPATFULL on STN

AB The present invention provides methods for the treatment of obesity using sterol or 5.alpha.-stanol absorption inhibitors and compositions and therapeutic combinations including sterol or 5.alpha.-stanol absorption inhibitors and at least one obesity control medication.

AN 2003:173582 USPATFULL

TI Methods and therapeutic combinations for the treatment of obesity using sterol absorption inhibitors

IN Davis, Harry R., Berkeley Heights, NJ, UNITED STATES
Ress, Rudyard J., Flemington, NJ, UNITED STATES
Strony, John T., Lebanon, NJ, UNITED STATES
Veltri, Enrico P., Princeton, NJ, UNITED STATES

PA Schering Corporation (U.S. corporation)

PI US 2003119428 A1 20030626

AI US 2002-247397 A1 20020919 (10)

RLI Continuation-in-part of Ser. No. US 2002-166942, filed on 11 Jun 2002, PENDING

PRAI US 2001-323840P 20010921 (60)

DT Utility

FS APPLICATION

LREP SCHERING-PLOUGH CORPORATION, PATENT DEPARTMENT (K-6-1, 1990), 2000 GALLOPING HILL ROAD, KENILWORTH, NJ, 07033-0530
CLMN Number of Claims: 35
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 3027
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
SUMM . . . of Formula (I) useful in the compositions, therapeutic combinations and methods of the present invention is represented by Formula (II) (**ezetimibe**) below: ##STR3##
SUMM . . . MEVACOR.RTM. which is available from Merck & Co.), pravastatin (for example PRAVACHOL.RTM. which is available from Bristol Meyers Squibb), fluvastatin, **simvastatin** (for example ZOCOR.RTM. which is available from Merck & Co.), atorvastatin, cerivastatin, CI-981, rivastatin (sodium 7-(4-fluorophenyl)-2,6-diisopropyl-5-methoxymethylpyridin-3-yl)-3,5-dihydroxy-6-heptanoate) and pitavastatin (such as. . . NB-598 ((E)-N-ethyl-N-(6,6-dimethyl-2-hepten-4-ynyl)-3-[(3,3'-bithiophen-5-yl)methoxy]benzene-methanamine hydrochloride) and other sterol biosynthesis inhibitors such as DMP-565. Preferred HMG CoA reductase inhibitors include lovastatin, pravastatin and **simvastatin**. The most preferred HMG CoA reductase inhibitor is **simvastatin**.
SUMM [0397] Non-limiting examples of suitable bile acid sequestrants include **cholestyramine** (a styrene-divinylbenzene copolymer containing quaternary ammonium cationic groups capable of binding bile acids, such as QUESTRAN.RTM. or QUESTRAN LIGHT.RTM. **cholestyramine** which are available from Bristol-Myers Squibb), colestipol (a copolymer of diethylenetriamine and 1-chloro-2,3-epoxypropane, such as COLESTID.RTM. tablets which are available. . .
DETD . . . subjects and can be useful in the treatment and/or prevention of vascular conditions, such as vascular inflammation, atherosclerosis, hypercholesterolemia and **sitosterolemia**, stroke, obesity and lowering of plasma levels of cholesterol in subjects, in particular in humans.
IT **163222-33-1P** 163380-16-3P
(methods and therapeutic combinations for treatment of obesity using sterol absorption inhibitors)

L15 ANSWER 6 OF 14 USPATFULL on STN
AB Hypocholesterolemic substituted 2-azetidinone compounds of the formula: ##STR1##

are disclosed, as well as a methods of lowering cholesterol by administering said compounds, pharmaceutical compositions containing them, and the combination of a substituted 2-azetidinone cholesterol-lowering agent and a cholesterol biosynthesis inhibitor for the treatment and prevention of atherosclerosis.
AN 2003:153360 USPATFULL
TI Substituted 2-azetidinones useful as hypocholesterolemic agents
IN Ghosal, Anima, Edison, NJ, UNITED STATES
Zbaida, Shmuel, East Brunswick, NJ, UNITED STATES
Chowdhury, Swapan K., Warren, NJ, UNITED STATES
Iannucci, Robert M., Hampton, NJ, UNITED STATES
Feng, Wenqing, Chatham, NJ, UNITED STATES
Alton, Kevin B., Cedar Knolls, NJ, UNITED STATES
Patrick, James E., Belle Mead, NJ, UNITED STATES
Davis, Harry R., Berkeley Heights, NJ, UNITED STATES
PA Schering Corporation (U.S. corporation)
PI US 2003105028 A1 20030605
AI US 2002-166942 A1 20020611 (10)
RLI Continuation-in-part of Ser. No. US 2001-23295, filed on 17 Dec 2001, PENDING
PRAI US 2000-256875P 20001220 (60)
DT Utility

FS APPLICATION
LREP SCHERING-PLOUGH CORPORATION, PATENT DEPARTMENT (K-6-1, 1990), 2000 GALLOPING HILL ROAD, KENILWORTH, NJ, 07033-0530
CLMN Number of Claims: 36
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 1603
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

SUMM . . . dietary and/or pharmacological means leads to reductions in the incidence of death from cardiovascular disease." Davis, H. R., et al., " **Ezetimibe**, a potent cholesterol absorption inhibitor, inhibits the development of atherosclerosis in Apo knockout mice", 21 Arterioeoler. Thromb. Vasc. Biol. 2032-2038. . .

SUMM . . . halting of progression of one or more conditions, for example vascular conditions, such as hyperlipidaemia (for example atherosclerosis, hypercholesterolemia or **sitosterolemia**), vascular inflammation, stroke, diabetes, obesity and/or to reduce the level of sterol(s) (such as cholesterol) in the plasma. As used. . .

SUMM [0180] The compound of Formula III is a metabolite of **ezetimibe** (below): ##STR29##

SUMM . . . MEVACOR.RTM. which is available from Merck & Co.), pravastatin (for example PRAVACHOL.RTM. which is available from Bristol Meyers Squibb), fluvastatin, **simvastatin** (for example ZOCOR.RTM. which is available from Merck & Co.), atorvastatin, cerivastatin, CI-981, ZD4522, rivastatin (sodium 7-(4-fluorophenyl)-2,6-diisopropyl-5-methoxymethylpyridin-3-yl)-3,5-dihydroxy-6-heptanoate), rosuvastatin, pitavastatin (such. . . hydrochloride) and other sterol biosynthesis inhibitors such as DMP-565. Preferred HMG CoA reductase inhibitors include lovastatin, pravastatin, fluvastatin, atorvastatin and **simvastatin**. The most preferred HMG CoA reductase inhibitor is **simvastatin**.

SUMM . . . invention can further comprise one or more peroxisome proliferator-activated receptor (PPAR) activators (such as fibrates), bile acid sequestrants (such as **cholestyramine**), ileal bile acid transport ("IBAT") inhibitors (such as benzothiepines) or apical sodium co-dependent bile acid transport ("ASBT") inhibitors, nicotinic acid. . .

SUMM . . . and can be useful in the treatment and/or prevention of conditions, for example vascular conditions, such as atherosclerosis, hypercholesterolemia and **sitosterolemia**, stroke, obesity and lowering of plasma levels of cholesterol in mammals, in particular in humans.

CLM What is claimed is:

. . . composition according to claim 21, wherein the cholesterol biosynthesis inhibitor is selected from the group consisting of lovastatin, pravastatin, fluvastatin, **simvastatin**, atorvastatin, L-659,699, squalestatin 1, NB-598, pitavastatin and ZD4522.

23. The pharmaceutical composition according to claim 22, wherein the cholesterol biosynthesis inhibitor is **simvastatin**.

26. The method according to claim 25, wherein the cholesterol biosynthesis inhibitor is selected from the group consisting of lovastatin, pravastatin, fluvastatin, **simvastatin**, atorvastatin, L-659,699, squalestatin 1, NB-598, pitavastatin and ZD4522.

27. The method according to claim 26, wherein the cholesterol biosynthesis inhibitor is **simvastatin**.

31. The pharmaceutical composition according to claim 30, wherein the cholesterol biosynthesis inhibitor is selected from the group consisting of lovastatin, pravastatin, fluvastatin, **simvastatin**,

atorvastatin, L-659,699, squalestatin 1, NB-598, pitavastatin and ZD4522.

32. The pharmaceutical composition according to claim 31, wherein the cholesterol biosynthesis inhibitor is **simvastatin**.

35. The method according to claim 34, wherein the cholesterol biosynthesis inhibitor is selected from the group consisting of lovastatin, pravastatin, fluvastatin, **simvastatin**, atorvastatin, L-659,699, squalestatin 1, NB-598, pitavastatin and ZD4522.

36. The method according to claim 35, wherein the cholesterol biosynthesis inhibitor is **simvastatin**.

IT 29066-42-0, L 659699 75330-75-5, Lovastatin **79902-63-9**, Simvastatin 81093-37-0, Pravastatin 93957-54-1, Fluvastatin 131060-14-5, NB-598 134523-00-5, Atorvastatin 142561-96-4, Squalestatin 1 147098-20-2, ZD4522 147511-69-1, Pitavastatin
(prepn. of azetidinone glucuronide derivs. and their use as hypocholesterolemic agents combined with a cholesterol biosynthesis inhibitor for treating diabetes, obesity, vascular conditions, and lowering plasma sterol concns.)

IT **163222-33-1P**, Sch 58235 536709-33-8P
(prepn. of azetidinone glucuronide derivs. and their use as hypocholesterolemic agents for treating diabetes, obesity, vascular conditions, and lowering plasma sterol concns.)

L15 ANSWER 7 OF 14 USPATFULL on STN

AB The present invention provides compositions, therapeutic combinations and methods including: (a) at least one sterol absorption inhibitor and (b) at least one cardiovascular agent different from the sterol absorption inhibitor, which can be useful for treating vascular conditions, obesity, diabetes and lowering plasma levels of sterols.

AN 2003:100110 USPATFULL

TI Combinations of sterol absorption inhibitor(s) with cardiovascular agent(s) for the treatment of vascular conditions

IN Kosoglou, Teddy, Jamison, PA, UNITED STATES
Ress, Rudyard J., Flemington, NJ, UNITED STATES
Strony, John T., Lebanon, NJ, UNITED STATES
Veltri, Enrico P., Princeton, NJ, UNITED STATES
Hauer, William, Warren, NJ, UNITED STATES

PA Schering Corporation (U.S. corporation)

PI US 2003069221 A1 20030410

AI US 2002-57339 A1 20020125 (10)

PRAI US 2001-323842P 20010921 (60)
US 2001-264396P 20010126 (60)
US 2001-264600P 20010126 (60)
US 2001-264275P 20010126 (60)

DT Utility

FS APPLICATION

LREP SCHERING-PLOUGH CORPORATION, PATENT DEPARTMENT (K-6-1, 1990), 2000 GALLOPING HILL ROAD, KENILWORTH, NJ, 07033-0530

CLMN Number of Claims: 49

ECL Exemplary Claim: 1

DRWN No Drawings

LN.CNT 3423

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

SUMM . . . in a therapeutically effective amount to treat vascular conditions such as atherosclerosis, hyperlipidaemia (including but not limited to hypercholesterolaemia, hypertriglyceridaemia, **sitosterolemia**), hypertension, vascular inflammation, angina, cardiac arrhythmias, stroke, as well as diabetes, obesity, and/or to reduce the level of sterol(s) in. . .

SUMM . . . agent(s) and sterol absorption inhibitor(s), to prevent or treat a vascular condition, such as hyperlipidaemia (for example atherosclerosis, hypercholesterolemia or **sitosterolemia**), stroke, diabetes, obesity and/or reduce the level of sterol(s) in the plasma. As used herein, "vascular" comprises cardiovascular, cerebrovascular and. . .

SUMM . . . of Formula (I) useful in the compositions, therapeutic combinations and methods of the present invention is represented by Formula (II) (**ezetimibe**) below: ##STR2##

SUMM . . . MEVACOR.RTM. which is available from Merck & Co.), pravastatin (for example PRAVACHOL.RTM. which is available from Bristol Meyers Squibb), fluvastatin, **simvastatin** (for example ZOCOR.RTM. which is available from Merck & Co.), atorvastatin, cerivastatin, rosuvastatin, rivastatin (sodium 7-(4-fluorophenyl)-2,6-diisopropyl-5-methoxymethylpyridin-3-yl)-3,5-dihydroxy-6-heptanoate, CI-981 and pitavastatin (such. . . NB-598 ((E)--N-ethyl-N-(6,6-dimethyl-2-hepten-4-ynyl)-3-[(3,3'-bithiophen-5-yl)methoxy]benzene-methanamine hydrochloride) and other sterol biosynthesis inhibitors such as DMP-565. Preferred HMG CoA reductase inhibitors include lovastatin, pravastatin and **simvastatin**. The most preferred HMG CoA reductase inhibitor is **simvastatin**.

SUMM . . . Preferably the cholesterol biosynthesis inhibitor comprises one or more HMG CoA reductase inhibitors, such as, for example, lovastatin, pravastatin and/or **simvastatin**.

SUMM [0395] Non-limiting examples of suitable bile acid sequestrants include **cholestyramine** (a styrene-divinylbenzene copolymer containing quaternary ammonium cationic groups capable of binding bile acids, such as QUESTRAN.TM. or QUESTRAN LIGHTS.RTM. **cholestyramine** which are available from Bristol-Myers Squibb), colestipol (a copolymer of diethylenetriamine and 1-chloro-2,3-epoxypropane, such as COLESTID.RTM. tablets which are available. . .

DETD . . . below, and can be useful in the treatment and/or prevention of vascular conditions, such as vascular inflammation, atherosclerosis, hypercholesterolemia and **sitosterolemia**, stroke, obesity and lowering of plasma levels of cholesterol in mammals, in particular in humans.

CLM What is claimed is:

. . . 37. The composition according to claim 36 wherein the at least one HMG CoA reductase inhibitor comprises lovastatin, pravastatin, fluvastatin, **simvastatin**, atorvastatin, rosuvastatin, rivastatin, cerivastatin and mixtures thereof.

38. The composition according to claim 37, wherein the at least one HMG CoA reductase inhibitor comprises **simvastatin**.

IT **163222-33-1P**
(combinations of nicotinic acid and derivs. and azetidine sterol absorption inhibitor(s) for treatment of vascular indications)

IT 59-67-6, Nicotinic acid, biological studies 637-07-0, Clofibrate 943-45-3D, Fibric acid, derivs. 5868-05-3, Niceritrol **11041-12-6**, Cholestyramine 15351-13-0, Nicofuranose 23288-49-5, Probucol 25812-30-0, Gemfibrozil 30299-08-2, Clinofibrate 41859-67-0, Bezafibrate 49562-28-9, Fenofibrate 50925-79-6, Colestipol 51037-30-0, Acipimox 52214-84-3, Ciprofibrate 69047-39-8, Binifibrate 75330-75-5, Lovastatin **79902-63-9**, Simvastatin 81093-37-0, Pravastatin 93957-54-1, Fluvastatin 96609-16-4, Lifibrol 134523-00-5, Atorvastatin 145599-86-6, Cerivastatin
(combinations of nicotinic acid and derivs. and azetidine sterol absorption inhibitor(s) for treatment of vascular indications)

L15 ANSWER 8 OF 14 USPATFULL on STN

AB The present invention provides compositions, therapeutic combinations and methods including: (a) at least one bile acid sequestrant; and (b)

at least one substituted azetidinone or substituted .beta.-lactam sterol absorption inhibitor which can be useful for treating vascular conditions, diabetes, obesity and lowering plasma levels of sterols.

AN 2003:78061 USPATFULL

TI Combinations of bile acid sequestrant(s) and sterol absorption inhibitor(s) and treatments for vascular indications

IN Davis, Harry R., Berkeley Heights, NJ, UNITED STATES
Kosoglou, Teddy, Jamison, PA, UNITED STATES

PA Schering Corporation (U.S. corporation)

PI US 2003053981 A1 20030320

AI US 2002-57534 A1 20020125 (10)

PRAI US 2001-264600P 20010126 (60)
US 2001-323842P 20010921 (60)

DT Utility

FS APPLICATION

LREP SCHERING-PLOUGH CORPORATION, PATENT DEPARTMENT (K-6-1, 1990), 2000 GALLOPING HILL ROAD, KENILWORTH, NJ, 07033-0530

CLMN Number of Claims: 81

ECL Exemplary Claim: 1

DRWN No Drawings

LN.CNT 4194

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

SUMM [0006] Bile acid sequestrants, such as **cholestyramine** and colestipol, can lower intrahepatic cholesterol and promote the synthesis of apo B/E (LDL) receptors which bind LDL from plasma. . .

SUMM [0223] Non-limiting examples of suitable bile acid sequestrants include **cholestyramine** (a styrene-divinylbenzene copolymer containing quaternary ammonium cationic groups capable of binding bile acids, such as QUESTRAN.RTM. or QUESTRAN LIGHT.RTM. which. . .

SUMM . . . halting of progression of one or more conditions, for example vascular conditions, such as hyperlipidemia (for example atherosclerosis, hypercholesterolemia or **sitosterolemia**), vascular inflammation, stroke, diabetes, obesity and/or to reduce the level of sterol(s) (such as cholesterol) in the plasma.

SUMM . . . inhibitor(s), to prevent or treat a condition, for example a vascular condition, such as hyperlipidaemia (for example atherosclerosis, hypercholesterolemia or **sitosterolemia**), stroke, diabetes, obesity and/or reduce the level of sterol(s) in the plasma. As used herein, "vascular" comprises cardiovascular, cerebrovascular and. . .

SUMM [0260] In a preferred embodiment, a sterol inhibitor of Formula (I) (**ezetimibe**) useful in the compositions, therapeutic combinations and methods of the present invention is represented by Formula (II) below: ##STR32##

SUMM . . . MEVACOR.RTM. which is available from Merck & Co.), pravastatin (for example PRAVACHOL.RTM. which is available from Bristol Meyers Squibb), fluvastatin, **simvastatin** (for example ZOCOR.RTM. which is available from Merck & Co.), atorvastatin, cerivastatin, CI-981 and pitavastatin (such as NK-104 of Negma. . . NB-598 ((E)-N-ethyl-N-(6,6-dimethyl-2-hepten-4-ynyl)-3-[(3,3'-bithiophen-5-yl)methoxy]benzene-methanamine hydrochloride) and other sterol biosynthesis inhibitors such as DMP-565. Preferred HMG CoA reductase inhibitors include lovastatin, pravastatin and **simvastatin**. The most preferred HMG CoA reductase inhibitor is **simvastatin**.

SUMM . . . acid sequestrants and one or more cholesterol biosynthesis inhibitors. In this embodiment, preferably the bile acid sequestrant is selected from **cholestyramine** and/or colestipol. Preferably the cholesterol biosynthesis inhibitor comprises one or more HMG CoA reductase inhibitors, such as, for example, lovastatin, pravastatin and/or **simvastatin**. More preferably, the composition or treatment comprises the compound of Formula (II) in combination with **simvastatin** and **cholestyramine** or colestipol.

SUMM . . . in a therapeutically effective amount to treat vascular conditions such as atherosclerosis, hyperlipidaemia (including but not

limited to hypercholesterolaemia, hypertriglyceridaemia, **sitosterolemia**), stroke, diabetes, obesity, and/or reduce the level of sterol(s) in the plasma. The compositions and treatments can be administered by. . .

DETD . . . be coadministered with a tablet, capsule, etc. comprising a dosage of Active Compound II, for example a tablet of QUESTRAN.RTM. **cholestyramine** as described above.

DETD . . . cholesterol in mammals, and can be useful in the treatment and/or prevention of vascular conditions, such as atherosclerosis, hypercholesterolemia and **sitosterolemia**, stroke, diabetes, obesity and lowering of plasma levels of cholesterol in mammals, in particular in mammals.

DETD [0653] in combination with the bile acid sequestrant **cholestyramine** would have additive efficacy. Compound XII can be prepared as shown in Example 9 of U.S. Pat. No. 5,688,787, which. . .

DETD . . . hour after they were gavaged with corn oil as a Control, compound of Formula (XII) (3 mg/kg of body weight), **cholestyramine** (1 g/kg of body weight), or the compound of Formula (XII) combined with **cholestyramine** as described in Table 1 below. Two hours later, blood and liver samples were collected from each hamster. The blood. . . of liver)

Control	4945 .+-. 644	8035 .+-. 1611
Compound XII (3 mg/kg of body weight)	1438 .+-. 455 (-71%)	3755 .+-. 923 (-53%)
Cholestyramine (1 g/kg of body weight)	836 .+-. 320 (-83%)	3300 .+-. 1252 (-60%)
Compound XII (3 mg/kg) + **Cholestyramine** (1 g/kg of body weight)	478 .+-. 101 (-90%)	1196 .+-. 247 (-85%)

DETD . . . reduced plasma and liver [.sup.14C]-cholesterol levels by 71% and 53%, respectively (see Table 1). Administration of the specified dosage of **cholestyramine** alone reduced plasma and liver [.sup.14C]-cholesterol levels by 83% and 60%, respectively. The specified combination of Compound XII and **cholestyramine** resulted in reductions in plasma and hepatic (liver) [.sup.14C]-cholesterol levels by 90% and 85%, respectively (see Table 1). These results indicate that the combination of the cholesterol absorption inhibitor, Compound XII, and the bile acid sequestrant, **cholestyramine**, may have additional effects on treating hypercholesterolemia by reducing both plasma and hepatic cholesterol levels.

CLM What is claimed is:

. . . composition according to claim 1, wherein the at least one bile acid sequestrant is selected from the group consisting of **cholestyramine**, colestipol, colesevelam hydrochloride and mixtures thereof.

3. The composition according to claim 2, wherein the at least one bile acid sequestrant comprises **cholestyramine**.

10. The composition according to claim 9, wherein the at least one HMG CoA reductase inhibitor is selected from the group consisting of lovastatin, pravastatin, fluvastatin, **simvastatin**, atorvastatin, cerivastatin and mixtures thereof.

11. The composition according to claim 10, wherein the at least one HMG CoA reductase inhibitor is **simvastatin**.

IT **163222-33-1P**
(combinations of nicotinic acid and derivs. and azetidine sterol absorption inhibitor(s) for treatment of vascular indications)

IT 59-67-6, Nicotinic acid, biological studies 637-07-0, Clofibrate

943-45-3D, Fibric acid, derivs. 5868-05-3, Niceritrol
11041-12-6, Cholestyramine 15351-13-0, Nicofuranose
23288-49-5, Probucol 25812-30-0, Gemfibrozil 30299-08-2, Clinofibrate
41859-67-0, Bezafibrate 49562-28-9, Fenofibrate 50925-79-6,
Colestipol 51037-30-0, Acipimox 52214-84-3, Ciprofibrate
69047-39-8, Binifibrate 75330-75-5, Lovastatin **79902-63-9**,
Simvastatin 81093-37-0, Pravastatin 93957-54-1, Fluvastatin
96609-16-4, Lifibrol 134523-00-5, Atorvastatin 145599-86-6,
Cerivastatin
(combinations of nicotinic acid and derivs. and azetidine sterol absorption inhibitor(s) for treatment of vascular indications)

L15 ANSWER 9 OF 14 CAPLUS COPYRIGHT 2003 ACS on STN
AB The invention discloses the use of sterol absorption-inhibiting compds., pharmaceutical compns. thereof, therapeutic combinations, and their use in combination with other lipid-lowering agents to treat or prevent **sitosterolemia** and/or to lower the concn. of sterol(s) other than cholesterol in plasma or tissue of a mammal. Methods of treating or preventing vascular disease and coronary events also are provided. The methodol. and compns. of the invention use substituted azetidinone compds., e.g. I (prepn. described).
AN 2002:574926 CAPLUS
DN 137:135094
TI The use of substituted azetidinone compounds for the treatment of **sitosterolemia**
IN Davis, Harry R.
PA Schering Corporation, USA
SO PCT Int. Appl., 105 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2002058696	A2	20020801	WO 2002-US1195	20020125
	WO 2002058696	A3	20030313		
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, HR, HU, ID, IL, IN, IS, JP, KG, KR, KZ, LC, LK, LR, LT, LU, LV, MA, MD, MG, MK, MN, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UZ, VN, YU, ZA, ZM, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	US 2002169134	A1	20021114	US 2002-57629	20020125
PRAI	US 2001-264645P	P	20010126		

OS MARPAT 137:135094
TI The use of substituted azetidinone compounds for the treatment of **sitosterolemia**
AB The invention discloses the use of sterol absorption-inhibiting compds., pharmaceutical compns. thereof, therapeutic combinations, and their use in combination with other lipid-lowering agents to treat or prevent **sitosterolemia** and/or to lower the concn. of sterol(s) other than cholesterol in plasma or tissue of a mammal. Methods of treating or preventing vascular disease and coronary events also are provided. The methodol. and compns. of the invention use substituted azetidinone compds., e.g. I (prepn. described).
ST azetidinone deriv prepn **sitosterolemia** treatment; noncholesterol sterol redn azetidinone deriv; vascular disease coronary event treatment azetidinone deriv
IT Apolipoproteins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(E, apoE knockout mouse; azetidinone derivs. for treatment of

sitosterolemia)
IT Antiarteriosclerotics
(antiatherosclerotics; azetidinone derivs. for treatment of **sitosterolemia**)
IT Antiarteriosclerotics
Arteriosclerosis
Atherosclerosis
Blood vessel, disease
Cardiovascular agents
Cardiovascular system, disease
Drug delivery systems
Human
Hypolipemic agents
(azetidinone derivs. for treatment of **sitosterolemia**)
IT Sterols
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(azetidinone derivs. for treatment of **sitosterolemia**)
IT Sequestering agents
(bile acid; azetidinone derivs. for treatment of **sitosterolemia**)
IT Drug delivery systems
(capsules; azetidinone derivs. for treatment of **sitosterolemia**)
IT Artery, disease
(coronary; azetidinone derivs. for treatment of **sitosterolemia**)
IT Liver
(hepatic sitosterol accumulation; azetidinone derivs. for treatment of **sitosterolemia**)
IT Lipoproteins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(low-d.; azetidinone derivs. for treatment of **sitosterolemia**)
IT Lipids, biological studies
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(metabolic disorders; azetidinone derivs. for treatment of **sitosterolemia**)
IT Embryophyta
(phytosterols; azetidinone derivs. for treatment of **sitosterolemia**)
IT Natural products
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(phytosterols; azetidinone derivs. for treatment of **sitosterolemia**)
IT Drug delivery systems
(prodrugs; azetidinone derivs. for treatment of **sitosterolemia**)
IT Bile acids
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(sequestrants; azetidinone derivs. for treatment of **sitosterolemia**)
IT Sterols
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(stanols, 5.alpha.-; azetidinone derivs. for treatment of **sitosterolemia**)
IT Drug delivery systems
(tablets; azetidinone derivs. for treatment of **sitosterolemia**)
IT Biological transport
(uptake; azetidinone derivs. for treatment of **sitosterolemia**)
IT 57-88-5, Cholesterol, biological studies
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(LDL; azetidinone derivs. for treatment of **sitosterolemia**)
IT 80-97-7, Cholestanol 83-45-4, Sitostanol 83-46-5 83-48-7, Stigmasterol 474-60-2, Campestanol 474-62-4, Campesterol 23290-26-8,

Avenasterol
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(azetidinone derivs. for treatment of **sitosterolemia**)

IT **163222-33-1P**
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(azetidinone derivs. for treatment of **sitosterolemia**)

IT **11041-12-6**, **Cholestyramine** 50925-79-6, Colestipol
75330-75-5, Lovastatin **79902-63-9**, **Simvastatin**
81093-37-0, Pravastatin 93957-54-1, Fluvastatin 134523-00-5, Atorvastatin 147511-69-1, Itavastatin 163222-33-1D, prodrug derivs. 182815-44-7, Colesevelam hydrochloride 287714-41-4, Rosuvastatin 438576-91-1 438576-91-1D, derivs. 438576-92-2 438576-92-2D, prodrug derivs. 444313-49-9 444313-50-2 444313-51-3 444313-53-5 444313-55-7 444313-57-9 444313-59-1 444313-60-4 444313-61-5 444313-62-6
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(azetidinone derivs. for treatment of **sitosterolemia**)

IT 9028-35-7, HMG-CoA reductase
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(inhibitors; azetidinone derivs. for treatment of **sitosterolemia**)

IT 163222-32-0P 163380-15-2P 191330-56-0P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. and reaction; azetidinone derivs. for treatment of **sitosterolemia**)

IT 112022-81-8 112022-83-0 133472-27-2, 4-Fluorophenylzinc chloride
RL: RCT (Reactant); RACT (Reactant or reagent)
(reaction; azetidinone derivs. for treatment of **sitosterolemia**)

L15 ANSWER 10 OF 14 USPATFULL on STN

AB The present invention provides compositions, therapeutic combinations and methods including: (a) at least one peroxisome proliferator-activated receptor activator; and (b) at least one substituted azetidinone or substituted .beta.-lactam sterol absorption inhibitor which can be useful for treating vascular conditions, diabetes, obesity and lowering plasma levels of sterols.

AN 2002:336849 USPATFULL

TI Sterol absorption inhibitor compositions

IN Cho, Wing-Kee Philip, Princeton, NJ, UNITED STATES
Davis, Harry R., Berkeley Heights, NJ, UNITED STATES
Kosoglou, Teddy, Jamison, PA, UNITED STATES
Picard, Gilles J., Braine L'Alleud, BELGIUM

PI US 2002192203 A1 20021219

AI US 2002-136968 A1 20020501 (10)

RLI Division of Ser. No. US 2002-57323, filed on 25 Jan 2002, PENDING

PRAI US 2001-264396P 20010126 (60)
US 2001-323839P 20010921 (60)

DT Utility

FS APPLICATION

LREP SCHERING-PLOUGH CORPORATION, PATENT DEPARTMENT (K-6-1, 1990), 2000 GALLOPING HILL ROAD, KENILWORTH, NJ, 07033-0530

CLMN Number of Claims: 101

ECL Exemplary Claim: 1

DRWN No Drawings

LN.CNT 4987

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

SUMM . . . halting of progression of one or more conditions, for example vascular conditions, such as hyperlipidaemia (for example atherosclerosis, hypercholesterolemia or **sitosterolemia**),

vascular inflammation, stroke, diabetes, obesity and/or to reduce the level of sterol(s) (such as cholesterol) in the plasma.

SUMM . . . inhibitor(s), to prevent or treat a condition, for example a vascular condition, such as hyperlipidaemia (for example atherosclerosis, hypercholesterolemia or **sitosterolemia**), vascular inflammation, stroke, diabetes, obesity and/or reduce the level of sterol(s) (such as cholesterol) in the plasma. As used herein,. . .

SUMM . . . of Formula (I) useful in the compositions, therapeutic combinations and methods of the present invention is represented by Formula (II) (**ezetimibe**) below: ##STR31##

SUMM . . . MEVACOR.RTM. which is available from Merck & Co.), pravastatin (for example PRAVACHOL.RTM. which is available from Bristol Meyers Squibb), fluvastatin, **simvastatin** (for example ZOCOR.RTM. which is available from Merck & Co.), atorvastatin, cerivastatin, CI-981, rivastatin (sodium 7-(4-fluorophenyl)-2,6-diisopropyl-5-methoxymethylpyridin-3-yl)-3,5-dihydroxy-6-heptanoate), rosuvastatin, pitavastatin (such as. . . NB-598 ((E)--N-ethyl-N-(6,6-dimethyl-2-hepten-4-ynyl)-3-[(3,3'-bithiophen-5-yl)methoxy]benzene-methanamine hydrochloride) and other sterol biosynthesis inhibitors such as DMP-565. Preferred HMG CoA reductase inhibitors include lovastatin, pravastatin and **simvastatin**. The most preferred HMG CoA reductase inhibitor is **simvastatin**.

SUMM . . . Preferably the cholesterol biosynthesis inhibitor comprises one or more HMG CoA reductase inhibitors, such as, for example, lovastatin, pravastatin and/or **simvastatin**. More preferably, the composition or treatment comprises the compound of Formula (II) in combination with **simvastatin** and gemfibrozil or fenofibrate.

SUMM . . . bind LDL from plasma to further reduce cholesterol levels in the blood. Non-limiting examples of suitable bile acid sequestrants include **cholestyramine** (a styrene-divinylbenzene copolymer containing quaternary ammonium cationic groups capable of binding bile acids, such as QUESTRAN.RTM. or QUESTRAN LIGHT.RTM. **cholestyramine** which are available from Bristol-Myers Squibb), colestipol (a copolymer of diethylenetriamine and 1-chloro-2,3-epoxypropane, such as COLESTID.RTM. tablets which are available. . .

SUMM . . . treat one or more conditions, for example vascular conditions such as atherosclerosis, hyperlipidaemia (including but not limited to hypercholesterolemia, hypertriglyceridaemia, **sitosterolemia**), vascular inflammation, stroke, diabetes, obesity, and/or reduce the level of sterol(s) in the plasma. The compositions and treatments can be. . .

DETD . . . and can be useful in the treatment and/or prevention of conditions, for example vascular conditions, such as atherosclerosis, hypercholesterolemia and **sitosterolemia**, stroke, obesity and lowering of plasma levels of cholesterol in mammals, in particular in mammals.

CLM What is claimed is:

. . . 15, wherein the at least one HMG CoA reductase inhibitor is selected from the group consisting of lovastatin, pravastatin, fluvastatin, **simvastatin**, atorvastatin, rosuvastatin, cerivastatin and mixtures thereof.

17. The composition according to claim 16, wherein the at least one HMG CoA reductase inhibitor is **simvastatin**.

18. The composition according to claim 12, further comprising **simvastatin**.

46. The composition according to claim 45, wherein the at least one HMG CoA reductase inhibitor is **simvastatin**.

52. The method of claim 51, wherein the HMG CoA reductase inhibitor is **simvastatin**.

IT **163222-33-1P**
(combinations of nicotinic acid and derivs. and azetidine sterol absorption inhibitor(s) for treatment of vascular indications)
IT 59-67-6, Nicotinic acid, biological studies 637-07-0, Clofibrate 943-45-3D, Fibric acid, derivs. 5868-05-3, Niceritrol **11041-12-6**, Cholestyramine 15351-13-0, Nicofuranose 23288-49-5, Probucol 25812-30-0, Gemfibrozil 30299-08-2, Clinofibrate 41859-67-0, Bezafibrate 49562-28-9, Fenofibrate 50925-79-6, Colestipol 51037-30-0, Acipimox 52214-84-3, Ciprofibrate 69047-39-8, Binifibrate 75330-75-5, Lovastatin **79902-63-9**, Simvastatin 81093-37-0, Pravastatin 93957-54-1, Fluvastatin 96609-16-4, Lifibrol 134523-00-5, Atorvastatin 145599-86-6, Cerivastatin
(combinations of nicotinic acid and derivs. and azetidine sterol absorption inhibitor(s) for treatment of vascular indications)

L15 ANSWER 11 OF 14 USPATFULL on STN
AB The present invention provides compositions, therapeutic combinations and methods including: (a) at least one of nicotinic acid or derivatives thereof; and (b) at least one substituted azetidinone or substituted .beta.-lactam sterol absorption inhibitor which can be useful for treating vascular conditions, diabetes, obesity and lowering plasma levels of sterols.
AN 2002:323139 USPATFULL
TI Combinations of nicotinic acid and derivatives thereof and sterol absorption inhibitor(s) and treatments for vascular indications
IN Davis, Harry R., Berkeley Heights, NJ, UNITED STATES
Kosoglou, Teddy, Jamison, PA, UNITED STATES
PA Schering Corporation (U.S. corporation)
PI US 2002183305 A1 20021205
AI US 2002-57646 A1 20020125 (10)
PRAI US 2001-264275P 20010126 (60)
US 2001-323842P 20010921 (60)
DT Utility
FS APPLICATION
LREP SCHERING-PLOUGH CORPORATION, PATENT DEPARTMENT (K-6-1, 1990), 2000 GALLOPING HILL ROAD, KENILWORTH, NJ, 07033-0530
CLMN Number of Claims: 81
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 4256
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
SUMM . . . halting of progression of one or more conditions, for example vascular conditions, such as hyperlipidemia (for example atherosclerosis, hypercholesterolemia or **sitosterolemia**), vascular inflammation, stroke, diabetes, obesity and/or to reduce the level of sterol(s) (such as cholesterol) in the plasma.
SUMM . . . inhibitor(s), to prevent or treat a condition, for example a vascular condition, such as hyperlipidaemia (for example atherosclerosis, hypercholesterolemia or **sitosterolemia**), stroke, diabetes, obesity and/or reduce the level of sterol(s) in the plasma. As used herein, "vascular" comprises cardiovascular, cerebrovascular and. . .
SUMM [0262] In a preferred embodiment, a sterol inhibitor of Formula (I) (**ezetimibe**) useful in the compositions, therapeutic combinations and methods of the present invention is represented by Formula (II) below: ##STR31##
SUMM . . . MEVACOR.RTM. which is available from Merck & Co.), pravastatin (for example PRAVACHOL.RTM. which is available from Bristol Meyers Squibb), fluvastatin, **simvastatin** (for example ZOCOR.RTM. which is available from Merck & Co.), atorvastatin, cerivastatin, CI-981, and pitavastatin (such as NK-104 of Negma. . . NB-598 ((E)-N-ethyl-N-(6,6-dimethyl-2-hepten4-ynyl)-3-[(3,3'-bithiophen-5-yl)methoxy]benzene-methanamine hydrochloride) and other sterol

biosynthesis inhibitors such as DMP-565. Preferred HMG CoA reductase inhibitors include lovastatin, pravastatin and **simvastatin**. The most preferred HMG CoA reductase inhibitor is **simvastatin**.

SUMM . . . Preferably the cholesterol biosynthesis inhibitor comprises one or more HMG CoA reductase inhibitors, such as, for example, lovastatin, pravastatin and/or **simvastatin**. More preferably, the composition or treatment comprises the compound of Formula (II) in combination with **simvastatin** and nicotinic acid or acipimox.

SUMM [0593] Non-limiting examples of suitable bile acid sequestrants include **cholestyramine** (a styrene-divinylbenzene copolymer containing quaternary ammonium cationic groups capable of binding bile acids, such as QUESTRAN.RTM. or QUESTRAN LIGHT.RTM. which. . .

SUMM . . . in a therapeutically effective amount to treat vascular conditions such as atherosclerosis, hyperlipidaemia (including but not limited to hypercholesterolaemia, hypertriglyceridaemia, **sitosterolemia**), stroke, diabetes, obesity, and/or reduce the level of sterol(s) in the plasma. The compositions and treatments can be administered by. . .

DETD . . . cholesterol in mammals, and can be useful in the treatment and/or prevention of vascular conditions, such as atherosclerosis, hypercholesterolemia and **sitosterolemia**, diabetes, obesity and lowering of plasma levels of cholesterol in mammals, in particular in mammals.

CLM What is claimed is:

. . . 8, wherein the at least one HMG CoA reductase inhibitor is selected from the group consisting of lovastatin, pravastatin, fluvastatin, **simvastatin**, atorvastatin, cerivastatin and mixtures thereof.

10. The composition according to claim 9, wherein the at least one HMG CoA reductase inhibitor is **simvastatin**.

15. The composition according to claim 14, wherein the at least one bile acid sequestrant is selected from the group consisting of **cholestyramine** and colestipol.

IT **163222-33-1P**
(combinations of nicotinic acid and derivs. and azetidine sterol absorption inhibitor(s) for treatment of vascular indications)

IT 59-67-6, Nicotinic acid, biological studies 637-07-0, Clofibrate 943-45-3D, Fibric acid, derivs. 5868-05-3, Niceritrol **11041-12-6**, Cholestyramine 15351-13-0, Nicofuranose 23288-49-5, Probucol 25812-30-0, Gemfibrozil 30299-08-2, Clinofibrate 41859-67-0, Bezafibrate 49562-28-9, Fenofibrate 50925-79-6, Colestipol 51037-30-0, Acipimox 52214-84-3, Ciprofibrate 69047-39-8, Binifibrate 75330-75-5, Lovastatin **79902-63-9**, Simvastatin 81093-37-0, Pravastatin 93957-54-1, Fluvastatin 96609-16-4, Lifibrol 134523-00-5, Atorvastatin 145599-86-6, Cerivastatin
(combinations of nicotinic acid and derivs. and azetidine sterol absorption inhibitor(s) for treatment of vascular indications)

L15 ANSWER 12 OF 14 USPATFULL on STN

AB The present invention is directed to the use of sterol absorption inhibiting compounds, pharmaceutical compositions thereof, therapeutic combinations and their use in combination with other lipid lowering agents to treat or prevent **sitosterolemia** and/or to lower the concentration of sterol(s) other than cholesterol in plasma or tissue of a mammal. Methods of treating or preventing vascular disease and coronary events also are provided.

AN 2002:301589 USPATFULL

TI Use of substituted azetidinone compounds for the treatment of **sitosterolemia**

IN Davis, Harry R., Berkeley Heights, NJ, UNITED STATES

PA Schering Corporation (U.S. corporation)

PI US 2002169134 A1 20021114
AI US 2002-57629 A1 20020125 (10)
PRAI US 2001-264645P 20010126 (60)
DT Utility
FS APPLICATION
LREP SCHERING-PLOUGH CORPORATION, PATENT DEPARTMENT (K-6-1, 1990), 2000 GALLOPING HILL ROAD, KENILWORTH, NJ, 07033-0530
CLMN Number of Claims: 58
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 3321
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
TI Use of substituted azetidinone compounds for the treatment of **sitosterolemia**
AB . . . compounds, pharmaceutical compositions thereof, therapeutic combinations and their use in combination with other lipid lowering agents to treat or prevent **sitosterolemia** and/or to lower the concentration of sterol(s) other than cholesterol in plasma or tissue of a mammal. Methods of treating. . .
SUMM [0002] The present invention provides methods and pharmaceutical compositions for treating or preventing **sitosterolemia** by administering to a mammal in need of such treatment an effective amount of at least one treatment composition comprising. . .
SUMM [0003] **Sitosterolemia** is a genetic lipid storage disorder characterized by increased levels of sitosterol and other plant sterols in the plasma and other tissues due to increased non-selective intestinal absorption of sterols and decreased hepatic removal. Individuals having **sitosterolemia** can exhibit one or more of the following conditions: tendon and tuberous xanthomas, arthritis, hemolytic episodes, accelerated atherosclerosis and myocardial. . . can die at an early age due to extensive coronary atherosclerosis. See Nguyen et al., "Regulation of cholesterol biosynthesis in **sitosterolemia**: effects of lovastatin, **cholestyramine**, and dietary sterol restriction", Vol 32, Journal of Lipid Research, pp. 1941-1948, (1991), incorporated by reference herein.
SUMM [0004] **Sitosterolemia** can be treated with bile acid sequestrants (such as **cholestyramine**, colesevelam hydrochloride and colestipol), however, these compounds have a tendency to cause constipation in patients and therefore compliance with this. . .
SUMM [0006] An improved treatment for **sitosterolemia** is needed which can reduce the concentration of sterols in plasma and tissues and inhibit associated debilitating physical effects. Also,. . .
SUMM [0007] The present invention provides a method of treating or preventing **sitosterolemia**, comprising administering to a mammal in need of such treatment an effective amount of at least one sterol absorption inhibitor,. . .
SUMM [0008] In another embodiment, the present invention provides a method of treating or preventing **sitosterolemia**, comprising administering to a mammal in need of such treatment: (1) an effective amount of at least one sterol absorption. . .
SUMM [0009] In another embodiment, the present invention provides a method of treating or preventing **sitosterolemia** comprising administering to a mammal in need of such treatment: (1) an effective amount of at least one sterol absorption. . .
SUMM [0010] Other embodiments of the present invention include pharmaceutical compositions for the treatment or prevention of **sitosterolemia** comprising an effective amount of the compositions or combinations used in the methods described above in a pharmaceutically acceptable carrier.
SUMM [0017] The present invention provides methods, pharmaceutical compositions and combinations for treating or preventing **sitosterolemia** and conditions or symptoms associated with **sitosterolemia** such as are discussed above. Another aspect of the present invention provides methods, pharmaceutical compositions and

combinations for reducing the. . . be useful in the treatment and/or prevention of vascular conditions or disease, such as vascular inflammation, arteriosclerosis, atherosclerosis, hypercholesterolemia and **sitosterolemia**, and cardiovascular events, stroke and/or obesity.

SUMM . . . inhibitor of Formula (VII) useful in the compositions, combinations and methods of the present invention is represented by Formula (VII) (**ezetimibe**) below: ##STR42##

SUMM [0351] Non-limiting examples of suitable bile acid sequestrants include **cholestyramine** (a styrene-divinylbenzene copolymer containing quaternary ammonium cationic groups capable of binding bile acids, such as QUESTRAN.RTM. or QUESTRAN LIGHT.RTM. which. . .

SUMM . . . for use in the treatment compositions of the present invention include HMG CoA reductase inhibitors such as lovastatin, pravastatin, fluvastatin, **simvastatin**, atorvastatin, rosuvastatin and itavastatin. Preferred HMG CoA reductase inhibitors include lovastatin, atorvastatin and **simvastatin**. The most preferred HMG CoA reductase inhibitors are atorvastatin and **simvastatin**.

SUMM . . . Formula (VIII) in combination with a bile acid sequestrant. In this embodiment, preferably the bile acid sequestrant is selected from **cholestyramine**, colesevelam hydrochloride and colestipol. Preferably, the treatment composition comprises one or more bile acid sequestrants such as, for example, **cholestyramine**, colesevelam hydrochloride and colestipol in combination with a compound of Formula (VIII) ##STR55##

SUMM . . . inhibitors. Preferably, the treatment composition comprises one or more HMG CoA reductase inhibitors such as, for example, lovastatin, atorvastatin and **simvastatin** in combination with a compound of Formula (VIII) ##STR56##

SUMM [0357] Still even more preferred, the treatment composition comprises compound of formula VIII in combination with atorvastatin and/or **simvastatin**.

SUMM . . . referred to herein as carrier materials). Because of their sterol absorption inhibitory activity, such pharmaceutical compositions possess utility in treating **sitosterolemia** and related disorders.

SUMM . . . can be administered to a mammal in need of such treatment in a pharmaceutically or therapeutically effective amount to treat **sitosterolemia** and/or reduce the level of sterol(s) in the plasma and tissues.

SUMM . . . therapeutic agents, such as sterol absorption inhibitor(s) and bile acid sequestrant(s) or other therapeutic vascular agents, to prevent or treat **sitosterolemia** and/or reduce the level of sterol(s) in the plasma and tissues. As used herein, "vascular" comprises cardiovascular, cerebrovascular and combinations. . .

SUMM . . . the intestinal absorption of sitosterol and can be useful in the treatment and/or prevention of vascular disease, arteriosclerosis, atherosclerosis and **sitosterolemia** in mammals, in particular in humans.

SUMM [0445] In another embodiment, the present invention provides a method of treating or preventing **sitosterolemia** comprising administering to a mammal in need of such treatment an effective amount of at least one sterol absorption inhibitor. . .

SUMM . . . and the second amount taken together in their totality comprise a therapeutically effective amount for the treatment or prevention of **sitosterolemia** in a mammal.

SUMM . . . be useful in the treatment and/or prevention of vascular conditions or disease, such as vascular inflammation, arteriosclerosis, atherosclerosis, hypercholesterolemia and **sitosterolemia**, and cardiovascular events, stroke and obesity.

DETD [0475] In a randomized multicenter, double-blind, placebo-controlled, 8-week trial, 37 human patients previously diagnosed with homozygous **sitosterolemia** were randomized to receive Compound VIII (n=30) or placebo (n=7):

DETD . . . T; Kwiterovich, Jr, P O, "Increased sitosterol absorption, decreased removal and expanded body pools compensate for reduced cholesterol synthesis in **sitosterolemia** with xanthomatosis", J Lipid Res, Vol. 30, pp 1319-30, (1989) and Lutjohann, D; Bjorkhem, I; Beil, U F, and von. . .

CLM What is claimed is:

1. A method of treating or preventing **sitosterolemia**, comprising administering to a mammal in need of such treatment an effective amount of at least one sterol absorption inhibitor,. . .

17. The method of claim 16, wherein the HMG-CoA reductase inhibitor is selected from the group consisting of **simvastatin**, lovastatin, pravastatin, fluvastatin, atorvastatin, rosuvastatin, itavastatin and mixtures thereof.

18. The method of claim 17, wherein the HMG-CoA reductase inhibitor is **simvastatin** or atorvastatin.

. . . The method of claim 22, wherein the HMG-CoA reductase inhibitor is selected from the group consisting of lovastatin, pravastatin, fluvastatin, **simvastatin**, atorvastatin, rosuvastatin, itavastatin and mixtures thereof.

24. A method of treating or preventing **sitosterolemia** comprising administering to a mammal in need of such treatment: (a) an effective amount of a sterol absorption inhibitor represented by Formula (VIII): ##STR90## and b) an effective amount of atorvastatin and/or **simvastatin**.

25. A pharmaceutical composition for the treatment or prevention of **sitosterolemia**, comprising an effective amount of the sterol absorption inhibitor used in the method of claim 1 in a pharmaceutically acceptable. . .

26. A pharmaceutical composition for the treatment or prevention of **sitosterolemia**, comprising an effective amount of the sterol absorption inhibitor used in the method of claim 8 in a pharmaceutically acceptable. . .

27. A pharmaceutical composition for the treatment or prevention of **sitosterolemia**, comprising an effective amount of the compound of Formula (VIII) ##STR91## in a pharmaceutically acceptable carrier.

28. A pharmaceutical composition for the treatment or prevention of **sitosterolemia**, comprising: a) an effective amount of the compound of Formula (VIII) ##STR92## and b) an effective amount of a lipid. . .

. . . composition of claim 29, wherein the HMG CoA reductase inhibitor is selected from the group consisting of lovastatin, pravastatin, fluvastatin, **simvastatin**, atorvastatin, rosuvastatin, itavastatin and mixtures thereof.

31. The composition of claim 30, wherein the HMG CoA reductase inhibitor is **simvastatin** or atorvastatin.

32. A method of treating or preventing **sitosterolemia**, comprising administering to a mammal in need of such treatment: (1) an effective amount of at least one sterol absorption. . .

33. A method of treating or preventing **sitosterolemia** comprising administering to a mammal in need of such treatment: (1) an effective amount of at least one sterol absorption. . .

42. The method of claim 41, wherein the HMG CoA reductase inhibitor is **simvastatin** or atorvastatin.

45. The method of claim 44, wherein the bile acid sequestrant is selected from the group consisting of **cholestyramine**, colesevelam hydrochloride, and colestipol.

46. A pharmaceutical composition for the treatment or prevention of **sitosterolemia**, comprising: a) an effective amount of the compound of Formula (VIII) ##STR95## and b) an effective amount of a bile. . .
47. The composition of claim 46, wherein the bile acid sequestrant is selected from the group consisting of **cholestyramine**, colesevelam hydrochloride, and colestipol.

. . . wherein the first amount and the second amount together comprise a therapeutically effective amount for the treatment or prevention of **sitosterolemia** in a mammal.

. . . wherein the first amount and the second amount together comprise a therapeutically effective amount for the treatment or prevention of **sitosterolemia** in a mammal.

IT **163222-33-1P**
(azetidinone derivs. for treatment of sitosterolemia)
IT **11041-12-6**, Cholestyramine 50925-79-6, Colestipol 75330-75-5, Lovastatin **79902-63-9**, Simvastatin 81093-37-0, Pravastatin 93957-54-1, Fluvastatin 134523-00-5, Atorvastatin 147511-69-1, Itavastatin **163222-33-1D**, prodrug derivs. 182815-44-7, Colesevelam hydrochloride 287714-41-4, Rosuvastatin 438576-91-1 438576-91-1D, derivs. 438576-92-2 438576-92-2D, prodrug derivs. 444313-49-9 444313-50-2 444313-51-3 444313-53-5 444313-55-7 444313-57-9 444313-59-1 444313-60-4 444313-61-5 444313-62-6
(azetidinone derivs. for treatment of sitosterolemia)

L15 ANSWER 13 OF 14 USPATFULL on STN
AB The present invention provides compositions, therapeutic combinations and methods including: (a) at least one peroxisome proliferator-activated receptor activator; and (b) at least one substituted azetidinone or substituted .beta.-lactam sterol absorption inhibitor which can be useful for treating vascular conditions, diabetes, obesity and lowering plasma levels of sterols.
AN 2002:273408 USPATFULL
TI Combinations of peroxisome proliferator-activated receptor (PPAR) activator(s) and sterol absorption inhibitor(s) and treatments for vascular indications
IN Davis, Harry R., Berkeley Heights, NJ, UNITED STATES
Kosoglou, Teddy, Jamison, PA, UNITED STATES
Picard, Gilles J., Brussels, BELGIUM
PA Schering Corporation (U.S. corporation)
PI US 2002151536 A1 20021017
AI US 2002-57323 A1 20020125 (10)
PRAI US 2001-264396P 20010126 (60)
US 2001-323839P 20010921 (60)
DT Utility
FS APPLICATION
LREP SCHERING-PLOUGH CORPORATION, PATENT DEPARTMENT (K-6-1, 1990), 2000 GALLOPING HILL ROAD, KENILWORTH, NJ, 07033-0530
CLMN Number of Claims: 101
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 5004
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
SUMM . . . halting of progression of one or more conditions, for example vascular conditions, such as hyperlipidaemia (for example atherosclerosis, hypercholesterolemia or **sitosterolemia**), vascular inflammation, stroke, diabetes, obesity and/or to reduce-the level of sterol(s) (such as cholesterol) in the plasma.
SUMM . . . inhibitor(s), to prevent or treat a condition, for example a vascular condition, such as hyperlipidaemia (for example

atherosclerosis, hypercholesterolemia or **sitosterolemia**), vascular inflammation, stroke, diabetes, obesity and/or reduce the level of sterol(s) (such as cholesterol) in the plasma. As used herein,. . .

SUMM . . . of Formula (I) useful in the compositions, therapeutic combinations and methods of the present invention is represented by Formula (II) (**ezetimibe**) below: ##STR33##

SUMM . . . MEVACOR.RTM. which is available from Merck & Co.), pravastatin (for example PRAVACHOL.RTM. which is available from Bristol Meyers Squibb), fluvastatin, **simvastatin** (for example ZOCOR.RTM. which is available from Merck & Co.), atorvastatin, cerivastatin, CI-981, rivastatin (sodium 7-(4-fluorophenyl)-2,6-diisopropyl-5-methoxymethylpyridin-3-yl)-3,5-dihydroxy-6-heptanoate), rosuvastatin, pitavastatin (such as. . . NB-598 ((E)--N-ethyl-N-(6,6-dimethyl-2-hepten-4-ynyl)-3-[(3,3'-bithiophen-5-yl)methoxy]benzene-methanamine hydrochloride) and other sterol biosynthesis inhibitors such as DMP-565. Preferred HMG CoA reductase inhibitors include lovastatin, pravastatin and **simvastatin**. The most preferred HMG CoA reductase inhibitor is **simvastatin**.

SUMM . . . Preferably the cholesterol biosynthesis inhibitor comprises one or more HMG CoA reductase inhibitors, such as, for example, lovastatin, pravastatin and/or **simvastatin**. More preferably, the composition or treatment comprises the compound of Formula (II) in combination with **simvastatin** and gemfibrozil or fenofibrate.

SUMM [0559] Non-limiting examples of suitable bile acid sequestrants include **cholestyramine** (a styrene-divinylbenzene copolymer containing quaternary ammonium cationic groups capable of binding bile acids, such as QUESTRAN.RTM. or QUESTRAN LIGHT.RTM. **cholestyramine** which are available from Bristol-Myers Squibb), colestipol (a copolymer of diethylenetriamine and 1-chloro-2,3-epoxypropane, such as COLESTID.RTM. tablets which are available. . .

SUMM . . . treat one or more conditions, for example vascular conditions such as atherosclerosis, hyperlipidaemia (including but not limited to hypercholesterolemia, hypertriglyceridaemia, **sitosterolemia**), vascular inflammation, stroke, diabetes, obesity, and/or reduce the level of sterol(s) in the plasma. The compositions and treatments can be. . .

DETD . . . and can be useful in the treatment and/or prevention of conditions, for example vascular conditions, such as atherosclerosis, hypercholesterolemia and **sitosterolemia**, stroke, obesity and lowering of plasma levels of cholesterol in mammals, in particular in mammals.

CLM What is claimed is:

. . . 15, wherein the at least one HMG CoA reductase inhibitor is selected from the group consisting of lovastatin, pravastatin, fluvastatin, **simvastatin**, atorvastatin, rosuvastatin, cerivastatin and mixtures thereof.

17. The composition according to claim 16, wherein the at least one HMG CoA reductase inhibitor is **simvastatin**.

18. The composition according to claim 12, further comprising **simvastatin**.

46. The composition according to claim 45, wherein the at least one HMG CoA reductase inhibitor is **simvastatin**.

52. The method of claim 51, wherein the HMG CoA reductase inhibitor is **simvastatin**.

IT **163222-33-1P**
(combinations of nicotinic acid and derivs. and azetidine sterol absorption inhibitor(s) for treatment of vascular indications)

IT 59-67-6, Nicotinic acid, biological studies 637-07-0, Clofibrate 943-45-3D, Fibric acid, derivs. 5868-05-3, Niceritrol

11041-12-6, Cholestyramine 15351-13-0, Nicofuranose
23288-49-5, Probucol 25812-30-0, Gemfibrozil 30299-08-2, Clinofibrate
41859-67-0, Bezafibrate 49562-28-9, Fenofibrate 50925-79-6,
Colestipol 51037-30-0, Acipimox 52214-84-3, Ciprofibrate
69047-39-8, Binifibrate 75330-75-5, Lovastatin **79902-63-9**,
Simvastatin 81093-37-0, Pravastatin 93957-54-1, Fluvastatin
96609-16-4, Lifibrol 134523-00-5, Atorvastatin 145599-86-6,
Cerivastatin
(combinations of nicotinic acid and derivs. and azetidine sterol absorption inhibitor(s) for treatment of vascular indications)

L15 ANSWER 14 OF 14 USPATFULL on STN

AB The present invention provides compositions, therapeutic combinations and methods including: (a) at least one sterol absorption inhibitor; and (b) at least one blood modifier, which can be useful for treating vascular conditions and lowering plasma levels of sterols.

AN 2002:266305 USPATFULL

TI Combinations of sterol absorption inhibitor(s) with blood modifier(s) for treating vascular conditions

IN Kosoglou, Teddy, Jamison, PA, UNITED STATES
Ress, Rudyard J., Flemington, NJ, UNITED STATES
Strony, John T., Lebanon, NJ, UNITED STATES
Veltri, Enrico P., Princeton, NJ, UNITED STATES

PA Schering Corporation (U.S. corporation)

PI US 2002147184 A1 20021010

AI US 2002-56680 A1 20020125 (10)

PRAI US 2001-324123P 20010921 (60)
US 2001-264396P 20010126 (60)
US 2001-264600P 20010126 (60)
US 2001-264275P 20010126 (60)

DT Utility

FS APPLICATION

LREP SCHERING-PLOUGH CORPORATION, PATENT DEPARTMENT (K-6-1, 1990), 2000 GALLOPING HILL ROAD, KENILWORTH, NJ, 07033-0530

CLMN Number of Claims: 48

ECL Exemplary Claim: 1

DRWN No Drawings

LN.CNT 3296

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

DETD . . . in a therapeutically effective amount to treat "vascular conditions" such as atherosclerosis, hyperlipidaemia (including but not limited to hypercholesterolaemia, hypertriglyceridaemia, **sitosterolemia**), vascular inflammation, hypertension, angina, cardiac arrhythmias, stroke, as well as conditions such diabetes, obesity, and/or to reduce the level of. . .

DETD . . . of Formula (I) useful in the compositions, therapeutic combinations and methods of the present invention is represented by Formula (II) (**ezetimibe**) below: ##STR3##

DETD . . . MEVACOR.RTM. which is available from Merck & Co.), pravastatin (for example PRAVACHOL.RTM. which is available from Bristol Meyers Squibb), fluvastatin, **simvastatin** (for example ZOCOR.RTM. which is available from Merck & Co.), atorvastatin, cerivastatin, rosuvastatin, rivastatin (sodium 7-(4-fluorophenyl)-2,6-diisopropyl-5-methoxymethylpyridin-3-yl)-3,5-dihydroxy-6-heptanoate CI-981 and pitavastatin (such. . . NB-598 ((E)--N-ethyl-N-(6,6-dimethyl-2-hepten-4-ynyl)-3-[(3,3'-bithiophen-5-yl)methoxy]benzene-methanamine hydrochloride) and other sterol biosynthesis inhibitors such as DMP-565. Preferred HMG CoA reductase inhibitors include lovastatin, pravastatin and **simvastatin**. The most preferred HMG CoA reductase inhibitor is **simvastatin**.

DETD . . . Preferably the cholesterol biosynthesis inhibitor comprises one or more HMG CoA reductase inhibitors, such as, for example, lovastatin, pravastatin and/or **simvastatin**.

DETD [0404] Non-limiting examples of suitable bile acid sequestrants include

cholestyramine (a styrene-divinylbenzene copolymer containing quaternary ammonium cationic groups capable of binding bile acids, such as QUESTRAN.RTM. or QUESTRAN LIGHT.RTM. **cholestyramine** which are available from Bristol-Myers Squibb), colestipol (a copolymer of diethylenetriamine and 1-chloro-2,3-epoxypropane, such as COLESTID.RTM. tablets which are available. . .

DETD . . . mammals, and can be useful in the treatment and/or prevention of vascular conditions, such as vascular inflammation, atherosclerosis, hypercholesterolemia and **sitosterolemia**, stroke, vascular conditions and lowering of plasma levels of cholesterol in mammals, in particular in humans.

CLM What is claimed is:

37. The composition according to claim 36, wherein the at least one HMG CoA reductase inhibitor is **simvastatin**.

IT **163222-33-1P**
(combinations of nicotinic acid and derivs. and azetidine sterol absorption inhibitor(s) for treatment of vascular indications)

IT 59-67-6, Nicotinic acid, biological studies 637-07-0, Clofibrate 943-45-3D, Fibric acid, derivs. 5868-05-3, Niceritrol **11041-12-6**, Cholestyramine 15351-13-0, Nicofuranose 23288-49-5, Probucol 25812-30-0, Gemfibrozil 30299-08-2, Clinofibrate 41859-67-0, Bezafibrate 49562-28-9, Fenofibrate 50925-79-6, Colestipol 51037-30-0, Acipimox 52214-84-3, Ciprofibrate 69047-39-8, Binifibrate 75330-75-5, Lovastatin **79902-63-9**, Simvastatin 81093-37-0, Pravastatin 93957-54-1, Fluvastatin 96609-16-4, Lifibrol 134523-00-5, Atorvastatin 145599-86-6, Cerivastatin
(combinations of nicotinic acid and derivs. and azetidine sterol absorption inhibitor(s) for treatment of vascular indications)

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> s ezetimibe/cn
L1            1 EZETIMIBE/CN

=> d

L1   ANSWER 1 OF 1  REGISTRY  COPYRIGHT 2003 ACS on STN
RN   163222-33-1  REGISTRY
CN   2-Azetidinone, 1-(4-fluorophenyl)-3-[(3S)-3-(4-fluorophenyl)-3-
     hydroxypropyl]-4-(4-hydroxyphenyl)-, (3R,4S)- (9CI)  (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN   2-Azetidinone, 1-(4-fluorophenyl)-3-[3-(4-fluorophenyl)-3-hydroxypropyl]-4-
     (4-hydroxyphenyl)-, [3R-[3.alpha.(S*),4.beta.]]-
OTHER NAMES:
CN   (-)-Sch 58235
CN   Ezetimibe
CN   Sch 58235
CN   Zetia
FS   STEREOSEARCH
MF   C24 H21 F2 N O3
CI   COM
SR   CA
LC   STN Files:   ADISINSIGHT, BIOBUSINESS, BIOSIS, BIOTECHNO, CA, CANCERLIT,
       CAPLUS, CASREACT, CHEMCATS, CIN, DIOGENES, DRUGNL, DRUGPAT, DRUGUPDATES,
       EMBASE, IPA, MEDLINE, MRCK*, PHAR, PROMT, SYNTHLINE, TOXCENTER, USAN,
       USPATFULL
         (*File contains numerically searchable property data)

Absolute stereochemistry.  Rotation (-).
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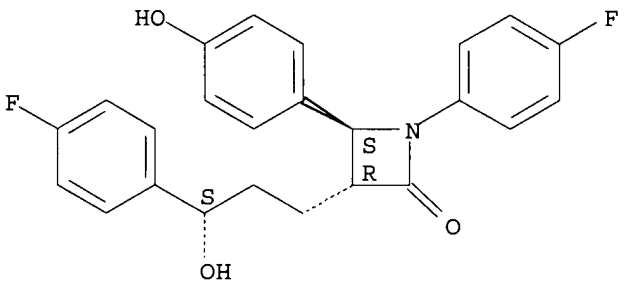


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**PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT**

             105 REFERENCES IN FILE CA (1907 TO DATE)
               2 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
             105 REFERENCES IN FILE CAPLUS (1907 TO DATE)


=> s cholestyramine/cn
L2            1 CHOLESTYRAMINE/CN

=> d

L2   ANSWER 1 OF 1  REGISTRY  COPYRIGHT 2003 ACS on STN
RN   11041-12-6  REGISTRY
CN   Cholestyramine (7CI, 8CI, 9CI)  (CA INDEX NAME)
OTHER NAMES:
CN   Cholestyramine chloride
CN   Cholestyramine resin
CN   Cholybar
CN   Colestyramin
```

CN Colestyramine
CN Cuemid
CN LoCholest
CN MK 135
CN Quantalan
CN Questran
CN Questran Light
DR 9007-26-5, 58391-37-0
MF Unspecified
CI PMS, COM, MAN
PCT Manual registration
LC STN Files: ADISNEWS, AGRICOLA, ANABSTR, BIOBUSINESS, BIOSIS, BIOTECHNO, CA, CABA, CANCERLIT, CAOLD, CAPLUS, CBNB, CEN, CHEMCATS, CHEMLIST, CIN, CSCHEM, DDFU, DIOGENES, DRUGU, EMBASE, IFICDB, IFIPAT, IFIUDB, IPA, MEDLINE, MRCK*, NIOSHTIC, PHARMASEARCH, PIRA, PROMT, RTECS*, TOXCENTER, USAN, USPAT2, USPATFULL, VETU
(*File contains numerically searchable property data)
Other Sources: EINECS**, NDSL**, TSCA**, WHO
(**Enter CHEMLIST File for up-to-date regulatory information)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
981 REFERENCES IN FILE CA (1907 TO DATE)
10 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
982 REFERENCES IN FILE CAPLUS (1907 TO DATE)
2 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

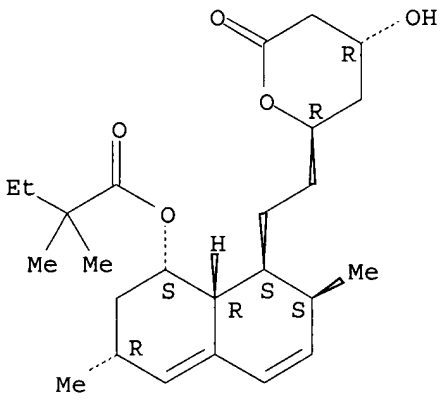
=> s simvastatin/cn
L3 1 SIMVASTATIN/CN

=> d

L3 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2003 ACS on STN
RN 79902-63-9 REGISTRY
CN Butanoic acid, 2,2-dimethyl-, (1S,3R,7S,8S,8aR)-1,2,3,7,8,8a-hexahydro-3,7-dimethyl-8-[2-[(2R,4R)-tetrahydro-4-hydroxy-6-oxo-2H-pyran-2-yl]ethyl]-1-naphthalenyl ester (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN Butanoic acid, 2,2-dimethyl-, 1,2,3,7,8,8a-hexahydro-3,7-dimethyl-8-[2-(tetrahydro-4-hydroxy-6-oxo-2H-pyran-2-yl)ethyl]-1-naphthalenyl ester, [1S-[1.alpha.,3.alpha.,7.beta.,8.beta.(2S*,4S*),8a.beta.]]-
OTHER NAMES:
CN (+)-Simvastatin
CN Cholestat
CN Denan
CN Eucor
CN Kolestevan
CN L 644128-000U
CN Lipex
CN Lipinorm
CN Liponorm
CN Lipovas
CN Lodales
CN MK 733
CN Modutrol
CN Nor-Vastina
CN Rechol
CN Simcor
CN Simovil
CN **Simvastatin**
CN Simvotin
CN Sinvacor
CN Sivastin
CN Statin

CN Synvinolin
CN Valemia
CN Velostatin
CN Zocor
CN Zocord
FS STEREOSEARCH
DR 98609-43-9, 118607-03-7
MF C25 H38 O5
CI COM
LC STN Files: ADISINSIGHT, ADISNEWS, AGRICOLA, ANABSTR, BEILSTEIN*, BIOBUSINESS, BIOSIS, BIOTECHNO, CA, CANCERLIT, CAPLUS, CASREACT, CBNB, CEN, CHEMCATS, CIN, CSCHEM, DDFU, DIOGENES, DRUGNL, DRUGPAT, DRUGU, DRUGUPDATES, EMBASE, IFICDB, IFIUDB, IPA, MEDLINE, MRCK*, NAPRALERT, PHAR, PHARMASEARCH, PROMT, RTECS*, SYNTHLINE, TOXCENTER, USAN, USPAT2, USPATFULL
(*File contains numerically searchable property data)
Other Sources: WHO

Absolute stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1683 REFERENCES IN FILE CA (1907 TO DATE)
38 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
1691 REFERENCES IN FILE CAPLUS (1907 TO DATE)

=> file caplus uspatfull embase medline biosis

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	20.90	21.95

FILE 'CAPLUS' ENTERED AT 15:29:26 ON 08 OCT 2003
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.

FILE 'USPATFULL' ENTERED AT 15:29:26 ON 08 OCT 2003

FILE 'EMBASE' ENTERED AT 15:29:26 ON 08 OCT 2003

FILE 'MEDLINE' ENTERED AT 15:29:26 ON 08 OCT 2003

FILE 'BIOSIS' ENTERED AT 15:29:26 ON 08 OCT 2003

```
=> s ezetimibe or 163222-33-1/rn
'RN' IS NOT A VALID FIELD CODE
'RN' IS NOT A VALID FIELD CODE
'RN' IS NOT A VALID FIELD CODE
L4          593 EZETIMIBE OR 163222-33-1/RN

=> s simvastatin or 79902-63-9/rn
'RN' IS NOT A VALID FIELD CODE
'RN' IS NOT A VALID FIELD CODE
'RN' IS NOT A VALID FIELD CODE
L5        14728 SIMVASTATIN OR 79902-63-9/RN

=> s cholestyramine or 11041-12-6/rn
'RN' IS NOT A VALID FIELD CODE
'RN' IS NOT A VALID FIELD CODE
'RN' IS NOT A VALID FIELD CODE
L6        10124 CHOLESTYRAMINE OR 11041-12-6/RN

=> s l4 and sitosterolemia
L7           25 L4 AND SITOSTEROLEMIA

=> dup rem l7
PROCESSING COMPLETED FOR L7
L8            21 DUP REM L7 (4 DUPLICATES REMOVED)

=> d l8 1-21 ab bib kwic

L8   ANSWER 1 OF 21  USPATFULL on STN
AB     The present invention provides therapeutic combinations and methods
       including at least one sterol or 5.alpha.-stanol absorption inhibitor
       that can be useful for treating xanthomas.
AN     2003:173961  USPATFULL
TI     Methods and therapeutic combinations for the treatment of xanthoma using
       sterol absorption inhibitors
IN     Davis, Harry R., Berkeley Heights, NJ, UNITED STATES
PA     Schering Corporation (U.S. corporation)
PI     US 2003119809      A1   20030626
AI     US 2002-247095     A1   20020919 (10)
PRAI   US 2001-323942P     20010921 (60)
DT     Utility
FS     APPLICATION
LREP   SCHERING-PLOUGH CORPORATION, PATENT DEPARTMENT (K-6-1, 1990), 2000
       GALLOPING HILL ROAD, KENILWORTH, NJ, 07033-0530
CLMN   Number of Claims: 23
ECL    Exemplary Claim: 1
DRWN   No Drawings
LN.CNT 2722
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
SUMM   . . . of Formula (I) useful in the compositions, therapeutic
       combinations and methods of the present invention is represented by
       Formula (II) (ezetimibe) below:   ##STR2##
DETD   . . . cholesterol in mammals, and can be useful in the treatment
       and/or prevention of vascular conditions, such as atherosclerosis,
       hypercholesterolemia and sitosterolemia, vascular
       inflammation, stroke, obesity and lowering of plasma levels of
       cholesterol in subjects, in particular in humans. As used herein,. . .
IT  163222-33-1P
        (sterol/5.alpha.-stanol absorption inhibitors for treatment of
        xanthoma, and use with other agents)

L8   ANSWER 2 OF 21  USPATFULL on STN
AB     The present invention relates to methods of treating or preventing
       cardiovascular conditions while preventing or minimizing muscular
```

degeneration side effects associated with certain HMG-CoA reductase inhibitors by coadministration of at least one sterol or 5.alpha.-stanol absorption inhibitor, pharmaceutically acceptable salts or solvates thereof, and at least one HMG-CoA reductase inhibitor, the latter being used sparingly in amounts insufficient to cause muscle degeneration.

AN 2003:173960 USPATFULL
TI Methods of treating or preventing cardiovascular conditions while preventing or minimizing muscular degeneration side effects
IN LeBeaut, Alexandre P., Morristown, NJ, UNITED STATES
Davis, Harry R., Berkeley Heights, NJ, UNITED STATES
PA Schering Corporation (U.S. corporation)
PI US 2003119808 A1 20030626
AI US 2002-246996 A1 20020919 (10)
PRAI US 2001-324121P 20010921 (60)
US 2002-351957P 20020125 (60)
DT Utility
FS APPLICATION
LREP SCHERING-PLOUGH CORPORATION, PATENT DEPARTMENT (K-6-1, 1990), 2000 GALLOPING HILL ROAD, KENILWORTH, NJ, 07033-0530
CLMN Number of Claims: 23
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 3092
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
SUMM . . . of Formula (I) useful in the compositions, therapeutic combinations and methods of the present invention is represented by Formula (II) (**ezetimibe**) below: ##STR2##
SUMM . . . can further be used to treat or prevent vascular disease or conditions (such as for example atherosclerosis, arteriosclerosis, hypercholesterolemia and/or **sitosterolemia**), cardiovascular events, hypertension, obesity, stroke, lowering of a concentration of a sterol in plasma of a mammal, reducing vascular inflammation. . .
SUMM . . . 5.alpha.-stanols in subjects and can be useful in the treatment and/or prevention of vascular conditions, such as atherosclerosis, hypercholesterolemia and **sitosterolemia**, stroke, obesity and lowering of plasma levels of sterols such as cholesterol or 5.alpha.-stanols in subject, in particular in humans.
IT **163222-33-1P**, Ezetimibe
(sterol or 5.alpha.-stanol absorption inhibitor; sterol or 5.alpha.-stanol absorption inhibitor and HMG-CoA reductase inhibitor for treating or preventing cardiovascular conditions while preventing muscle degeneration side effects)

L8 ANSWER 3 OF 21 USPATFULL on STN
AB The present invention provides compositions, therapeutic combinations and methods including: (a) at least one hormone replacement therapy composition; and (b) at least one sterol absorption inhibitor which can be useful for treating vascular conditions in post-menopausal women and lowering plasma levels of sterols or 5.alpha.-stanols.
AN 2003:173948 USPATFULL
TI Combinations of hormone replacement therapy composition(s) and sterol absorption inhibitor(s) and treatments for vascular conditions in post-menopausal women
IN Strony, John T., Lebanon, NJ, UNITED STATES
PA Schering Corporation (U.S. corporation)
PI US 2003119796 A1 20030626
AI US 2002-247085 A1 20020919 (10)
RLI Continuation-in-part of Ser. No. US 2002-166942, filed on 11 Jun 2002, PENDING
PRAI US 2001-324118P 20010921 (60)
DT Utility
FS APPLICATION
LREP SCHERING-PLOUGH CORPORATION, PATENT DEPARTMENT (K-6-1, 1990), 2000 GALLOPING HILL ROAD, KENILWORTH, NJ, 07033-0530

CLMN Number of Claims: 44
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 2932
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
SUMM . . . or halting of progression of the condition, for example a vascular condition, such as hyperlipidaemia (for example atherosclerosis, hypercholesterolemia or **sitosterolemia**), vascular inflammation, stroke, diabetes, obesity and/or reduce the level of sterol(s) (such as cholesterol) in the plasma of a patient,. . .
SUMM . . . of Formula (I) useful in the compositions, therapeutic combinations and methods of the present invention is represented by Formula (II) (**ezetimibe**) below: ##STR2##
DETD . . . 5.alpha.-stanol in subjects and can be useful in the treatment and/or prevention of vascular conditions, such as atherosclerosis, hypercholesterolemia and **sitosterolemia**, stroke, obesity and lowering of plasma levels of cholesterol in mammals, in particular in humans such as women, and preferably. . .
IT 163222-32-0P **163222-33-1P** 163380-15-2P
(synthesis of sterol absorption inhibitors for the combined use with hormone replacement therapy compns. and treatments for vascular conditions in post-menopausal women)

L8 ANSWER 4 OF 21 USPATFULL on STN
AB The present invention provides methods for treating or preventing vascular inflammation or for reducing blood levels of c-reactive protein by administering at least one sterol absorption inhibitor and/or at least one 5.alpha.-stanol absorption inhibitor.
AN 2003:173909 USPATFULL
TI Methods for treating or preventing vascular inflammation using sterol absorption inhibitor(s)
IN Davis, Harry R., Berkeley Heights, NJ, UNITED STATES
PA Schering Corporation (U.S. corporation)
PI US 2003119757 A1 20030626
AI US 2002-247032 A1 20020919 (10)
RLI Continuation-in-part of Ser. No. US 2002-166942, filed on 11 Jun 2002, PENDING
PRAI US 2001-323937P 20010921 (60)
DT Utility
FS APPLICATION
LREP SCHERING-PLOUGH CORPORATION, PATENT DEPARTMENT (K-6-1, 1990), 2000 GALLOPING HILL ROAD, KENILWORTH, NJ, 07033-0530
CLMN Number of Claims: 35
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 3032
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
SUMM . . . of Formula (I) useful in the compositions, therapeutic combinations and methods of the present invention is represented by Formula (II) (**ezetimibe**) below: ##STR3##
DETD . . . blood and can be useful in the treatment as well as prevention of vascular conditions, such as atherosclerosis, hypercholesterolemia and **sitosterolemia**, stroke, obesity and lower plasma levels of sterols and/or 5.alpha.-stanols in a subject, in particular in humans, such as phytosterols. . .
IT **163222-33-1P**, Ezetimibe
(sterol or 5.alpha.-stanol absorption inhibitor; sterol or 5.alpha.-stanol absorption inhibitor for reducing blood levels of C-reactive protein and treating or preventing vascular inflammation)

L8 ANSWER 5 OF 21 USPATFULL on STN
AB The present invention provides methods for the treatment of obesity using sterol or 5.alpha.-stanol absorption inhibitors and compositions and therapeutic combinations including sterol or 5.alpha.-stanol

absorption inhibitors and at least one obesity control medication.
AN 2003:173582 USPATFULL
TI Methods and therapeutic combinations for the treatment of obesity using sterol absorption inhibitors
IN Davis, Harry R., Berkeley Heights, NJ, UNITED STATES
Ress, Rudyard J., Flemington, NJ, UNITED STATES
Strony, John T., Lebanon, NJ, UNITED STATES
Veltri, Enrico P., Princeton, NJ, UNITED STATES
PA Schering Corporation (U.S. corporation)
PI US 2003119428 A1 20030626
AI US 2002-247397 A1 20020919 (10)
RLI Continuation-in-part of Ser. No. US 2002-166942, filed on 11 Jun 2002, PENDING
PRAI US 2001-323840P 20010921 (60)
DT Utility
FS APPLICATION
LREP SCHERING-PLOUGH CORPORATION, PATENT DEPARTMENT (K-6-1, 1990), 2000 GALLOPING HILL ROAD, KENILWORTH, NJ, 07033-0530
CLMN Number of Claims: 35
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 3027
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
SUMM . . . of Formula (I) useful in the compositions, therapeutic combinations and methods of the present invention is represented by Formula (II) (**ezetimibe**) below: ##STR3##
DETD . . . subjects and can be useful in the treatment and/or prevention of vascular conditions, such as vascular inflammation, atherosclerosis, hypercholesterolemia and **sitosterolemia**, stroke, obesity and lowering of plasma levels of cholesterol in subjects, in particular in humans.
IT **163222-33-1P** 163380-16-3P
(methods and therapeutic combinations for treatment of obesity using sterol absorption inhibitors)

L8 ANSWER 6 OF 21 USPATFULL on STN
AB Hypocholesterolemic substituted 2-azetidinone compounds of the formula: ##STR1##

are disclosed, as well as a methods of lowering cholesterol by administering said compounds, pharmaceutical compositions containing them, and the combination of a substituted 2-azetidinone cholesterol-lowering agent and a cholesterol biosynthesis inhibitor for the treatment and prevention of atherosclerosis.
AN 2003:153360 USPATFULL
TI Substituted 2-azetidinones useful as hypocholesterolemic agents
IN Ghosal, Anima, Edison, NJ, UNITED STATES
Zbaida, Shmuel, East Brunswick, NJ, UNITED STATES
Chowdhury, Swapan K., Warren, NJ, UNITED STATES
Iannucci, Robert M., Hampton, NJ, UNITED STATES
Feng, Wenqing, Chatham, NJ, UNITED STATES
Alton, Kevin B., Cedar Knolls, NJ, UNITED STATES
Patrick, James E., Belle Mead, NJ, UNITED STATES
Davis, Harry R., Berkeley Heights, NJ, UNITED STATES
PA Schering Corporation (U.S. corporation)
PI US 2003105028 A1 20030605
AI US 2002-166942 A1 20020611 (10)
RLI Continuation-in-part of Ser. No. US 2001-23295, filed on 17 Dec 2001, PENDING
PRAI US 2000-256875P 20001220 (60)
DT Utility
FS APPLICATION
LREP SCHERING-PLOUGH CORPORATION, PATENT DEPARTMENT (K-6-1, 1990), 2000 GALLOPING HILL ROAD, KENILWORTH, NJ, 07033-0530

CLMN Number of Claims: 36
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 1603
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
SUMM . . . dietary and/or pharmacological means leads to reductions in the incidence of death from cardiovascular disease." Davis, H. R., et al., " **Ezetimibe**, a potent cholesterol absorption inhibitor, inhibits the development of atherosclerosis in Apo knockout mice", 21 Arterioeoler. Thromb. Vasc. Biol. 2032-2038. . .
SUMM . . . halting of progression of one or more conditions, for example vascular conditions, such as hyperlipidaemia (for example atherosclerosis, hypercholesterolemia or **sitosterolemia**), vascular inflammation, stroke, diabetes, obesity and/or to reduce the level of sterol(s) (such as cholesterol) in the plasma. As used. . .
SUMM [0180] The compound of Formula III is a metabolite of **ezetimibe** (below): ##STR29##
SUMM . . . and can be useful in the treatment and/or prevention of conditions, for example vascular conditions, such as atherosclerosis, hypercholesterolemia and **sitosterolemia**, stroke, obesity and lowering of plasma levels of cholesterol in mammals, in particular in humans.
IT **163222-33-1P**, Sch 58235 536709-33-8P
(prepn. of azetidinone glucuronide derivs. and their use as hypocholesterolemic agents for treating diabetes, obesity, vascular conditions, and lowering plasma sterol concns.)

L8 ANSWER 7 OF 21 USPATFULL on STN
AB The present invention provides compositions, therapeutic combinations and methods including: (a) at least one sterol absorption inhibitor and (b) at least one cardiovascular agent different from the sterol absorption inhibitor, which can be useful for treating vascular conditions, obesity, diabetes and lowering plasma levels of sterols.
AN 2003:100110 USPATFULL
TI Combinations of sterol absorption inhibitor(s) with cardiovascular agent(s) for the treatment of vascular conditions
IN Kosoglou, Teddy, Jamison, PA, UNITED STATES
Ress, Rudyard J., Flemington, NJ, UNITED STATES
Strony, John T., Lebanon, NJ, UNITED STATES
Veltri, Enrico P., Princeton, NJ, UNITED STATES
Hauer, William, Warren, NJ, UNITED STATES
PA Schering Corporation (U.S. corporation)
PI US 2003069221 A1 20030410
AI US 2002-57339 A1 20020125 (10)
PRAI US 2001-323842P 20010921 (60)
US 2001-264396P 20010126 (60)
US 2001-264600P 20010126 (60)
US 2001-264275P 20010126 (60)
DT Utility
FS APPLICATION
LREP SCHERING-PLOUGH CORPORATION, PATENT DEPARTMENT (K-6-1, 1990), 2000 GALLOPING HILL ROAD, KENILWORTH, NJ, 07033-0530
CLMN Number of Claims: 49
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 3423
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
SUMM . . . in a therapeutically effective amount to treat vascular conditions such as atherosclerosis, hyperlipidaemia (including but not limited to hypercholesterolaemia, hypertriglyceridaemia, **sitosterolemia**), hypertension, vascular inflammation, angina, cardiac arrhythmias, stroke, as well as diabetes, obesity, and/or to reduce the level of sterol(s) in. . .
SUMM . . . agent(s) and sterol absorption inhibitor(s), to prevent or

treat a vascular condition, such as hyperlipidaemia (for example atherosclerosis, hypercholesterolemia or **sitosterolemia**), stroke, diabetes, obesity and/or reduce the level of sterol(s) in the plasma. As used herein, "vascular" comprises cardiovascular, cerebrovascular and. . .

SUMM . . . of Formula (I) useful in the compositions, therapeutic combinations and methods of the present invention is represented by Formula (II) (**ezetimibe**) below: ##STR2##

DETD . . . below, and can be useful in the treatment and/or prevention of vascular conditions, such as vascular inflammation, atherosclerosis, hypercholesterolemia and **sitosterolemia**, stroke, obesity and lowering of plasma levels of cholesterol in mammals, in particular in humans.

IT **163222-33-1P**
(combinations of nicotinic acid and derivs. and azetidine sterol absorption inhibitor(s) for treatment of vascular indications)

L8 ANSWER 8 OF 21 USPATFULL on STN

AB The present invention provides compositions, therapeutic combinations and methods including: (a) at least one bile acid sequestrant; and (b) at least one substituted azetidinone or substituted .beta.-lactam sterol absorption inhibitor which can be useful for treating vascular conditions, diabetes, obesity and lowering plasma levels of sterols.

AN 2003:78061 USPATFULL

TI Combinations of bile acid sequestrant(s) and sterol absorption inhibitor(s) and treatments for vascular indications

IN Davis, Harry R., Berkeley Heights, NJ, UNITED STATES
Kosoglou, Teddy, Jamison, PA, UNITED STATES

PA Schering Corporation (U.S. corporation)

PI US 2003053981 A1 20030320

AI US 2002-57534 A1 20020125 (10)

PRAI US 2001-264600P 20010126 (60)
US 2001-323842P 20010921 (60)

DT Utility

FS APPLICATION

LREP SCHERING-PLOUGH CORPORATION, PATENT DEPARTMENT (K-6-1, 1990), 2000 GALLOPING HILL ROAD, KENILWORTH, NJ, 07033-0530

CLMN Number of Claims: 81

ECL Exemplary Claim: 1

DRWN No Drawings

LN.CNT 4194

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

SUMM . . . halting of progression of one or more conditions, for example vascular conditions, such as hyperlipidemia (for example atherosclerosis, hypercholesterolemia or **sitosterolemia**), vascular inflammation, stroke, diabetes, obesity and/or to reduce the level of sterol(s) (such as cholesterol) in the plasma.

SUMM . . . inhibitor(s), to prevent or treat a condition, for example a vascular condition, such as hyperlipidaemia (for example atherosclerosis, hypercholesterolemia or **sitosterolemia**), stroke, diabetes, obesity and/or reduce the level of sterol(s) in the plasma. As used herein, "vascular" comprises cardiovascular, cerebrovascular and. . .

SUMM [0260] In a preferred embodiment, a sterol inhibitor of Formula (I) (**ezetimibe**) useful in the compositions, therapeutic combinations and methods of the present invention is represented by Formula (II) below: ##STR32##

SUMM . . . in a therapeutically effective amount to treat vascular conditions such as atherosclerosis, hyperlipidaemia (including but not limited to hypercholesterolaemia, hypertriglyceridaemia, **sitosterolemia**), stroke, diabetes, obesity, and/or reduce the level of sterol(s) in the plasma. The compositions and treatments can be administered by. . .

DETD . . . cholesterol in mammals, and can be useful in the treatment

and/or prevention of vascular conditions, such as atherosclerosis, hypercholesterolemia and **sitosterolemia**, stroke, diabetes, obesity and lowering of plasma levels of cholesterol in mammals, in particular in mammals.

IT **163222-33-1P**
(combinations of nicotinic acid and derivs. and azetidine sterol absorption inhibitor(s) for treatment of vascular indications)

L8 ANSWER 9 OF 21 EMBASE COPYRIGHT 2003 ELSEVIER INC. ALL RIGHTS RESERVED. on STN

AB OBJECTIVE: To review the primary literature describing the pharmacology of **ezetimibe** and clinical trials investigating its use in the management of hypercholesterolemia. DATA SOURCES: A MEDLINE search (1966-December 2002) was performed using SCH 48461, SCH 58235, **ezetimibe**, and 2-azetidinone as key words. English-language articles were identified and the references of these articles were used to further identify pertinent articles and abstracts. Given the paucity of published articles available on **ezetimibe**, many of the references cited are abstracts. STUDY SELECTION: All acquired articles that discussed the pharmacology, pharmacokinetics, chemistry, and clinical efficacy of **ezetimibe** were reviewed. DATA EXTRACTION: Articles were selected based on content regarding the medicinal chemistry, pharmacology, and clinical use of **ezetimibe**. DATA SYNTHESIS: **Ezetimibe**, approved for use in October 2002, belongs to a new class of antihyperlipidemic agents that uniquely inhibit the absorption of cholesterol by inhibiting the cholesterol transport system located within intestinal cell walls. In humans, **ezetimibe** reduced cholesterol absorption by >50%. In clinical trials, **ezetimibe** 10 mg/d reduced low-density lipoprotein cholesterol (LDL-C) by approximately 18% and further enhanced the LDL-C-lowering effect of statin medications by an additional 15-20%. In addition, **ezetimibe** lowered triglycerides about 5% and increased high-density lipoprotein cholesterol (HDL-C) approximately 3%. **Ezetimibe** is well tolerated. At present, no serious adverse effects have been directly attributable to **ezetimibe**. CONCLUSIONS: Based on the data currently available, it appears that **ezetimibe** has a potential role in the treatment of primary hypercholesterolemia; however further data are needed to determine its long-term tolerability and efficacy. The potential roles for **ezetimibe** include its concurrent use with a statin to further enhance the lowering of LDL-C. Other possible roles for **ezetimibe** include its concurrent use with a statin to permit a lowering of statin dosage to avoid statin-related complications or its use as monotherapy to treat hypercholesterolemia when statin use cannot be tolerated or is contraindicated. Outcome data demonstrating that cardiovascular morbidity and/or mortality are reduced by **ezetimibe** therapy have yet to be generated.

AN 2003213660 EMBASE

TI **Ezetimibe** for management of hypercholesterolemia.

AU Mauro V.F.; Tuckerman C.E.

CS C.E. Tuckerman, Pharmacy Services, Medical College of Ohio, 3000 Arlington Ave., Toledo, OH 43614-2589, United States. ctuckerman@mco.edu

SO Annals of Pharmacotherapy, (1 Jun 2003) 37/6 (839-848).
Refs: 64
ISSN: 1060-0280 CODEN: APHRER

CY United States

DT Journal; General Review

FS 018 Cardiovascular Diseases and Cardiovascular Surgery
037 Drug Literature Index
038 Adverse Reactions Titles

LA English

SL English; Spanish; French

TI **Ezetimibe** for management of hypercholesterolemia.

AB OBJECTIVE: To review the primary literature describing the pharmacology of **ezetimibe** and clinical trials investigating its use in the

management of hypercholesterolemia. DATA SOURCES: A MEDLINE search (1966-December 2002) was performed using SCH 48461, SCH 58235, **ezetimibe**, and 2-azetidinone as key words. English-language articles were identified and the references of these articles were used to further identify pertinent articles and abstracts. Given the paucity of published articles available on **ezetimibe**, many of the references cited are abstracts. STUDY SELECTION: All acquired articles that discussed the pharmacology, pharmacokinetics, chemistry, and clinical efficacy of **ezetimibe** were reviewed. DATA EXTRACTION: Articles were selected based on content regarding the medicinal chemistry, pharmacology, and clinical use of **ezetimibe**. DATA SYNTHESIS: **Ezetimibe**, approved for use in October 2002, belongs to a new class of antihyperlipidemic agents that uniquely inhibit the absorption of cholesterol by inhibiting the cholesterol transport system located within intestinal cell walls. In humans, **ezetimibe** reduced cholesterol absorption by >50%. In clinical trials, **ezetimibe** 10 mg/d reduced low-density lipoprotein cholesterol (LDL-C) by approximately 18% and further enhanced the LDL-C-lowering effect of statin medications by an additional 15-20%. In addition, **ezetimibe** lowered triglycerides about 5% and increased high-density lipoprotein cholesterol (HDL-C) approximately 3%. **Ezetimibe** is well tolerated. At present, no serious adverse effects have been directly attributable to **ezetimibe**. CONCLUSIONS: Based on the data currently available, it appears that **ezetimibe** has a potential role in the treatment of primary hypercholesterolemia; however further data are needed to determine its long-term tolerability and efficacy. The potential roles for **ezetimibe** include its concurrent use with a statin to further enhance the lowering of LDL-C. Other possible roles for **ezetimibe** include its concurrent use with a statin to permit a lowering of statin dosage to avoid statin-related complications or its. . . when statin use cannot be tolerated or is contraindicated. Outcome data demonstrating that cardiovascular morbidity and/or mortality are reduced by **ezetimibe** therapy have yet to be generated.

CT Medical Descriptors:

*hypercholesterolemia: DT, drug therapy

sitosterolemia: DT, drug therapy

metabolic disorder: DT, drug therapy

MEDLINE

cholesterol metabolism

cholesterol blood level

drug tolerability

cardiovascular disease

drug structure

drug half life

dose response

wrist disease: SI, side effect

thorax. . . SI, side effect

pharyngitis: SI, side effect

upper respiratory tract infection: SI, side effect

human

clinical trial

meta analysis

randomized controlled trial

double blind procedure

controlled study

review

priority journal

***ezetimibe: AE, adverse drug reaction**

***ezetimibe: CT, clinical trial**

***ezetimibe: AN, drug analysis**

***ezetimibe: CB, drug combination**

***ezetimibe: CM, drug comparison**

***ezetimibe: DO, drug dose**

***ezetimibe: DT, drug therapy**

***ezetimibe: PK, pharmacokinetics**
***ezetimibe: PD, pharmacology**
***ezetimibe: PO, oral drug administration**
*1,4 bis(4 methoxyphenyl) 3 (3 phenylpropyl) 2 azetidinone
*2 azetidinone derivative
low density lipoprotein cholesterol: EC, endogenous compound
statine
hydroxymethylglutaryl coenzyme. . .

RN (**ezetimibe**) 163222-33-1; (1,4 bis(4 methoxyphenyl) 3 (3 phenylpropyl) 2 azetidinone) 148260-92-8; (statine) 49642-07-1; (mevinolin) 75330-75-5; (simvastatin) 79902-63-9; (fenofibrate) 49562-28-9; (atorvastatin) 134523-00-5,. . .

L8 ANSWER 10 OF 21 EMBASE COPYRIGHT 2003 ELSEVIER INC. ALL RIGHTS RESERVED. on STN

AB Purpose of review: This review discusses recent progress in the role of ATP-binding cassette proteins ABCG5 and G8 in dietary sterol absorption, excretion and pathogenesis of cardiovascular disease. Recent findings: Identification of the genetic defect(s) underlying **sitosterolemia** has led to a renewed interest in the mechanisms of sterol absorption and biliary excretion. Mutations in ABCG5 (encoding sterolin-1) or ABCG8 (encoding sterolin-2) cause this disease. These proteins are thought to function by preventing dietary noncholesterol sterols from being retained by the body and for cholesterol excretion into bile. Summary: Despite improvements in treatments for hypercholesterolemia with cholesterol lowering agents, cardiovascular disease still remains highly prevalent. This has prompted many to consider that molecules other than cholesterol may be better biomarkers for this disease and targeting these more directly may allow us to develop more effective therapies. Ideally, if such a biomarker were also the bioactive molecule that is key to initiating/propagating the atherosclerosis pathogenic pathway, this would allow us to develop an optimal predictor and monitor of the disease process. One source of such molecules could come from our diet, with potential candidates such as noncholesterol sterols, oxysterols, oxidized sterols or some as yet unidentified dietary bioactive molecule. Nature has evolved a protective mechanism by which such molecules are kept out of the body, thereby reducing the negative effects of these compounds. The newly identified sterolin proteins involved in the absorption and excretion of dietary sterols may fit this bill. If so, we would speculate that a better biomarker may be lurking within their substrate specificities.

AN 2003320339 EMBASE

TI Genetic defenses against noncholesterol sterols.

AU Klett E.L.; Patel S.

CS E.L. Klett, Div. Endocrinol., Diabet./Med. G., Medical University of South Carolina, Strom Thurmond Building, 114 Doughty Street, Charleston, SC 29403, United States. klettel@musc.edu

SO Current Opinion in Lipidology, (2003) 14/4 (341-345).
Refs: 34
ISSN: 0957-9672 CODEN: COPLEU

CY United Kingdom

DT Journal; General Review

FS 003 Endocrinology
018 Cardiovascular Diseases and Cardiovascular Surgery
029 Clinical Biochemistry
030 Pharmacology
037 Drug Literature Index

LA English

SL English

AB . . . and G8 in dietary sterol absorption, excretion and pathogenesis of cardiovascular disease. Recent findings: Identification of the genetic defect(s) underlying **sitosterolemia** has led to a renewed interest in the mechanisms of sterol absorption and biliary excretion. Mutations in ABCG5 (encoding sterolin-1). . .

CT Medical Descriptors:

*atherosclerosis: . . . ET, etiology
*cardiovascular disease: PC, prevention
*gene
*ABCG5 gene
*ABCG8 gene
model
plant
liver cell
intestine cell
dietary intake
cholesterol metabolism
biliary excretion
bile acid synthesis
host resistance
gene mutation
genetic predisposition
disease predisposition
chromosome 2p
hypercholesterolemia: ET, etiology
sitosterolemia: ET, etiology
human
nonhuman
mouse
major clinical study
animal model
review
priority journal
*sterol
*phytosterol
*sitosterol
*sterolin 1
*sterolin 2
*ABC transporter
biological marker
oxysterol
C reactive protein: EC, endogenous compound
interleukin 6: EC, endogenous compound
homocysteine: EC, endogenous compound
cholesterol
antilipemic agent: PD, pharmacology
ezetimibe: PD, pharmacology
triacylglycerol
cholesterol ester
cholesterol acyltransferase
apolipoprotein B
messenger RNA
unclassified drug

RN (sitosterol) 19044-06-5, 83-46-5; (C reactive protein) 9007-41-4; (homocysteine) 454-28-4, 6027-13-0; (cholesterol) 57-88-5; (**ezetimibe**) 163222-33-1; (cholesterol acyltransferase) 9027-63-8

L8 ANSWER 11 OF 21 CAPLUS COPYRIGHT 2003 ACS on STN DUPLICATE 1

AB PURPOSE OF REVIEW: Cholesterol absorption is a selective process in that plant sterols and other non-cholesterol sterols are absorbed poorly or not at all. Recent research on the sterol efflux pumps ATP-binding cassette transporter G5 and ATP-binding cassette transporter G8 has not only provided an explanation for this selectivity, but also, together with the discovery of a new class of cholesterol absorption inhibitor, has yielded new insights into the mechanisms that potentially regulate the flux of cholesterol across the enterocyte. This review discusses these recent developments and their importance to the regulation of whole body cholesterol homeostasis. RECENT FINDINGS: ATP-binding cassette transporters G5/8 regulate plant sterol absorption and also the secretion into bile of cholesterol and non-cholesterol sterols. Loss of ATP-binding

cassette transporter G5/8 function results in **sitosterolemia**. **Ezetimibe**, a novel, potent and selective inhibitor of cholesterol absorption which is effective in milligram doses, lowers plasma plant sterol concns. in sitosterolemic subjects, thus suggesting that this drug might be inhibiting the activity of a putative sterol permease in the brush border membrane of the enterocyte that actively facilitates the uptake of cholesterol as well as other non-cholesterol sterols. SUMMARY: Intestinal cholesterol absorption represents a major route for the entry of cholesterol into the body's miscible pools and therefore can potentially impact the plasma LDL-cholesterol concn. The combined use of agents that inhibit the absorption and synthesis of cholesterol provides a powerful new approach to the prevention and treatment of atherosclerosis.

AN 2003:437076 CAPLUS
TI Sterol absorption by the small intestine
AU Turley, Stephen D.; Dietschy, John M.
CS Department of Internal Medicine, The University of Texas Southwestern Medical Center at Dallas, Dallas, TX, 75390-8887, USA
SO Current Opinion in Lipidology (2003), 14(3), 233-240
CODEN: COPLEU; ISSN: 0957-9672
PB Lippincott Williams & Wilkins
DT Journal
LA English
RE.CNT 60 THERE ARE 60 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

AB PURPOSE OF REVIEW: Cholesterol absorption is a selective process in that plant sterols and other non-cholesterol sterols are absorbed poorly or not at all. Recent research on the sterol efflux pumps ATP-binding cassette transporter G5 and ATP-binding cassette transporter G8 has not only provided an explanation for this selectivity, but also, together with the discovery of a new class of cholesterol absorption inhibitor, has yielded new insights into the mechanisms that potentially regulate the flux of cholesterol across the enterocyte. This review discusses these recent developments and their importance to the regulation of whole body cholesterol homeostasis. RECENT FINDINGS: ATP-binding cassette transporters G5/8 regulate plant sterol absorption and also the secretion into bile of cholesterol and non-cholesterol sterols. Loss of ATP-binding cassette transporter G5/8 function results in **sitosterolemia**. **Ezetimibe**, a novel, potent and selective inhibitor of cholesterol absorption which is effective in milligram doses, lowers plasma plant sterol concns. in sitosterolemic subjects, thus suggesting that this drug might be inhibiting the activity of a putative sterol permease in the brush border membrane of the enterocyte that actively facilitates the uptake of cholesterol as well as other non-cholesterol sterols. SUMMARY: Intestinal cholesterol absorption represents a major route for the entry of cholesterol into the body's miscible pools and therefore can potentially impact the plasma LDL-cholesterol concn. The combined use of agents that inhibit the absorption and synthesis of cholesterol provides a powerful new approach to the prevention and treatment of atherosclerosis.

L8 ANSWER 12 OF 21 CAPLUS COPYRIGHT 2003 ACS on STN DUPLICATE 2
AB A review. **Ezetimibe**, a synthetic 2-azetidinone, is the first of a new class of compds. that selectively inhibits the absorption of cholesterol and related plant sterols in the intestine. The drug, and its glucuronyl metabolite, are thought to inhibit a putative cholesterol transporter of enterocytes, located within the brush-border membrane of the small intestine. In large, randomized, placebo-controlled, 12-wk trials, **ezetimibe** reduced levels of low d. lipoprotein-cholesterol (LDL-C) by approx. 18%; triglyceride levels were reduced by approx. 6% in one trial but not another. **Ezetimibe** produced a modest increase in levels of high d. lipoprotein-cholesterol. Moreover, redns. in LDL-C and triglyceride levels were greater in patients treated with **ezetimibe** coadministered with a statin (lovastatin, pravastatin, atorvastatin or simvastatin), than with either of those agents given alone. The coadministration of the lowest statin dose and

ezetimibe produced similar LDL-C redns. to the administration of the highest statin dose alone. **Ezetimibe** also provided beneficial effects on plasma lipid levels when administered to patients with hypercholesterolemia already receiving a statin. **Ezetimibe** plus a statin reduced LDL-C levels more than the max. statin dose alone in a trial in patients with homozygous familial hypercholesterolemia and was effective in a placebo-controlled trial in patients with homozygous **sitosterolemia**. The drug was well tolerated in clin. studies conducted to date. In large, randomized, double-blind trials, **ezetimibe** had a similar tolerability profile to that of placebo. Coadministration of **ezetimibe** and a statin did not increase the incidence of adverse events related to statin monotherapy.

AN 2003:177555 CAPLUS
DN 138:362015
TI **Ezetimibe**
AU Darkes, Malcolm J. M.; Poole, Raewyn M.; Goa, Karen L.
CS Adis International Inc., Langhorne, PA, USA
SO American Journal of Cardiovascular Drugs (2003), 3(1), 67-76
CODEN: AJCDDJ; ISSN: 1175-3277
PB Adis International Ltd.
DT Journal; General Review
LA English
RE.CNT 68 THERE ARE 68 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

TI **Ezetimibe**

AB A review. **Ezetimibe**, a synthetic 2-azetidinone, is the first of a new class of compds. that selectively inhibits the absorption of cholesterol and related plant sterols in the intestine. The drug, and its glucuronyl metabolite, are thought to inhibit a putative cholesterol transporter of enterocytes, located within the brush-border membrane of the small intestine. In large, randomized, placebo-controlled, 12-wk trials, **ezetimibe** reduced levels of low d. lipoprotein-cholesterol (LDL-C) by approx. 18%; triglyceride levels were reduced by approx. 6% in one trial but not another. **Ezetimibe** produced a modest increase in levels of high d. lipoprotein-cholesterol. Moreover, redns. in LDL-C and triglyceride levels were greater in patients treated with **ezetimibe** coadministered with a statin (lovastatin, pravastatin, atorvastatin or simvastatin), than with either of those agents given alone. The coadministration of the lowest statin dose and **ezetimibe** produced similar LDL-C redns. to the administration of the highest statin dose alone. **Ezetimibe** also provided beneficial effects on plasma lipid levels when administered to patients with hypercholesterolemia already receiving a statin. **Ezetimibe** plus a statin reduced LDL-C levels more than the max. statin dose alone in a trial in patients with homozygous familial hypercholesterolemia and was effective in a placebo-controlled trial in patients with homozygous **sitosterolemia**. The drug was well tolerated in clin. studies conducted to date. In large, randomized, double-blind trials, **ezetimibe** had a similar tolerability profile to that of placebo. Coadministration of **ezetimibe** and a statin did not increase the incidence of adverse events related to statin monotherapy.

ST review anticholesteremic hypolipemic **ezetimibe** cholesterol lipid hypercholesterolemia

IT Development, mammalian postnatal
(adolescent; **ezetimibe** for patients with hypercholesterolemia)

IT Development, mammalian postnatal
(child; **ezetimibe** for patients with hypercholesterolemia)

IT Anticholesteremic agents
Human
Hypercholesterolemia
Hypolipemic agents
(**ezetimibe** for patients with hypercholesterolemia)

IT Lipids, biological studies

RL: BSU (Biological study, unclassified); BIOL (Biological study)
(**ezetimibe** for patients with hypercholesterolemia)

IT Drug interactions
(pharmacodynamic; **ezetimibe** for patients with hypercholesterolemia)

IT **163222-33-1**, **Ezetimibe**
RL: ADV (Adverse effect, including toxicity); DMA (Drug mechanism of action); PAC (Pharmacological activity); PKT (Pharmacokinetics); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**ezetimibe** for patients with hypercholesterolemia)

L8 ANSWER 13 OF 21 CAPLUS COPYRIGHT 2003 ACS on STN

AB The invention discloses the use of sterol absorption-inhibiting compds., pharmaceutical compns. thereof, therapeutic combinations, and their use in combination with other lipid-lowering agents to treat or prevent **sitosterolemia** and/or to lower the concn. of sterol(s) other than cholesterol in plasma or tissue of a mammal. Methods of treating or preventing vascular disease and coronary events also are provided. The methodol. and compns. of the invention use substituted azetidinone compds., e.g. I (prepn. described).

AN 2002:574926 CAPLUS
DN 137:135094

TI The use of substituted azetidinone compounds for the treatment of **sitosterolemia**

IN Davis, Harry R.
PA Schering Corporation, USA

SO PCT Int. Appl., 105 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2002058696	A2	20020801	WO 2002-US1195	20020125
WO 2002058696	A3	20030313		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, HR, HU, ID, IL, IN, IS, JP, KG, KR, KZ, LC, LK, LR, LT, LU, LV, MA, MD, MG, MK, MN, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UZ, VN, YU, ZA, ZM, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

US 2002169134	A1	20021114	US 2002-57629	20020125
PRAI US 2001-264645P	P	20010126		

OS MARPAT 137:135094

TI The use of substituted azetidinone compounds for the treatment of **sitosterolemia**

AB The invention discloses the use of sterol absorption-inhibiting compds., pharmaceutical compns. thereof, therapeutic combinations, and their use in combination with other lipid-lowering agents to treat or prevent **sitosterolemia** and/or to lower the concn. of sterol(s) other than cholesterol in plasma or tissue of a mammal. Methods of treating or preventing vascular disease and coronary events also are provided. The methodol. and compns. of the invention use substituted azetidinone compds., e.g. I (prepn. described).

ST azetidinone deriv prepn **sitosterolemia** treatment; noncholesterol sterol redn azetidinone deriv; vascular disease coronary event treatment azetidinone deriv

IT Apolipoproteins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(E, apoE knockout mouse; azetidinone derivs. for treatment of **sitosterolemia**)

IT Antiarteriosclerotics
(antiatherosclerotics; azetidinone derivs. for treatment of **sitosterolemia**)
IT Antiarteriosclerotics
Arteriosclerosis
Atherosclerosis
Blood vessel, disease
Cardiovascular agents
Cardiovascular system, disease
Drug delivery systems
Human
Hypolipemic agents
(azetidinone derivs. for treatment of **sitosterolemia**)
IT Sterols
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(azetidinone derivs. for treatment of **sitosterolemia**)
IT Sequestering agents
(bile acid; azetidinone derivs. for treatment of **sitosterolemia**)
IT Drug delivery systems
(capsules; azetidinone derivs. for treatment of **sitosterolemia**)
IT Artery, disease
(coronary; azetidinone derivs. for treatment of **sitosterolemia**)
IT Liver
(hepatic sitosterol accumulation; azetidinone derivs. for treatment of **sitosterolemia**)
IT Lipoproteins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(low-d.; azetidinone derivs. for treatment of **sitosterolemia**)
IT Lipids, biological studies
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(metabolic disorders; azetidinone derivs. for treatment of **sitosterolemia**)
IT Embryophyta
(phytosterols; azetidinone derivs. for treatment of **sitosterolemia**)
IT Natural products
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(phytosterols; azetidinone derivs. for treatment of **sitosterolemia**)
IT Drug delivery systems
(prodrugs; azetidinone derivs. for treatment of **sitosterolemia**)
IT Bile acids
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(sequestrants; azetidinone derivs. for treatment of **sitosterolemia**)
IT Sterols
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(stanols, 5.alpha.-; azetidinone derivs. for treatment of **sitosterolemia**)
IT Drug delivery systems
(tablets; azetidinone derivs. for treatment of **sitosterolemia**)
IT Biological transport
(uptake; azetidinone derivs. for treatment of **sitosterolemia**)
IT 57-88-5, Cholesterol, biological studies
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(LDL; azetidinone derivs. for treatment of **sitosterolemia**)
IT 80-97-7, Cholestanol 83-45-4, Sitostanol 83-46-5 83-48-7, Stigmasterol 474-60-2, Campestanol 474-62-4, Campesterol 23290-26-8, Avenasterol

RL: BSU (Biological study, unclassified); BIOL (Biological study)
(azetidinone derivs. for treatment of **sitosterolemia**)

IT **163222-33-1P**
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(azetidinone derivs. for treatment of **sitosterolemia**)

IT 11041-12-6, Cholestyramine 50925-79-6, Colestipol 75330-75-5, Lovastatin 79902-63-9, Simvastatin 81093-37-0, Pravastatin 93957-54-1, Fluvastatin 134523-00-5, Atorvastatin 147511-69-1, Itavastatin 163222-33-1D, prodrug derivs. 182815-44-7, Colesevelam hydrochloride 287714-41-4, Rosuvastatin 438576-91-1 438576-91-1D, derivs. 438576-92-2 438576-92-2D, prodrug derivs. 444313-49-9 444313-50-2 444313-51-3 444313-53-5 444313-55-7 444313-57-9 444313-59-1 444313-60-4 444313-61-5 444313-62-6
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(azetidinone derivs. for treatment of **sitosterolemia**)

IT 9028-35-7, HMG-CoA reductase
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(inhibitors; azetidinone derivs. for treatment of **sitosterolemia**)

IT 163222-32-0P 163380-15-2P 191330-56-0P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. and reaction; azetidinone derivs. for treatment of **sitosterolemia**)

IT 112022-81-8 112022-83-0 133472-27-2, 4-Fluorophenylzinc chloride
RL: RCT (Reactant); RACT (Reactant or reagent)
(reaction; azetidinone derivs. for treatment of **sitosterolemia**)

L8 ANSWER 14 OF 21 USPATFULL on STN

AB The present invention provides compositions, therapeutic combinations and methods including: (a) at least one peroxisome proliferator-activated receptor activator; and (b) at least one substituted azetidinone or substituted .beta.-lactam sterol absorption inhibitor which can be useful for treating vascular conditions, diabetes, obesity and lowering plasma levels of sterols.

AN 2002:336849 USPATFULL

TI Sterol absorption inhibitor compositions

IN Cho, Wing-Kee Philip, Princeton, NJ, UNITED STATES
Davis, Harry R., Berkeley Heights, NJ, UNITED STATES
Kosoglou, Teddy, Jamison, PA, UNITED STATES
Picard, Gilles J., Braine L'Alleud, BELGIUM

PI US 2002192203 A1 20021219
AI US 2002-136968 A1 20020501 (10)
RLI Division of Ser. No. US 2002-57323, filed on 25 Jan 2002, PENDING
PRAI US 2001-264396P 20010126 (60)
US 2001-323839P 20010921 (60)
DT Utility
FS APPLICATION
LREP SCHERING-PLOUGH CORPORATION, PATENT DEPARTMENT (K-6-1, 1990), 2000 GALLOPING HILL ROAD, KENILWORTH, NJ, 07033-0530
CLMN Number of Claims: 101
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 4987
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

SUMM . . . halting of progression of one or more conditions, for example vascular conditions, such as hyperlipidaemia (for example atherosclerosis, hypercholesterolemia or **sitosterolemia**), vascular inflammation, stroke, diabetes, obesity and/or to reduce the level of sterol(s) (such as cholesterol) in the plasma.

SUMM . . . inhibitor(s), to prevent or treat a condition, for example a vascular condition, such as hyperlipidaemia (for example atherosclerosis, hypercholesterolemia or **sitosterolemia**), vascular inflammation, stroke, diabetes, obesity and/or reduce the level of sterol(s) (such as cholesterol) in the plasma. As used herein,. . .

SUMM . . . of Formula (I) useful in the compositions, therapeutic combinations and methods of the present invention is represented by Formula (II) (**ezetimibe**) below: ##STR31##

SUMM . . . treat one or more conditions, for example vascular conditions such as atherosclerosis, hyperlipidaemia (including but not limited to hypercholesterolemia, hypertriglyceridaemia, **sitosterolemia**), vascular inflammation, stroke, diabetes, obesity, and/or reduce the level of sterol(s) in the plasma. The compositions and treatments can be. . .

DETD . . . and can be useful in the treatment and/or prevention of conditions, for example vascular conditions, such as atherosclerosis, hypercholesterolemia and **sitosterolemia**, stroke, obesity and lowering of plasma levels of cholesterol in mammals, in particular in mammals.

IT **163222-33-1P**
(combinations of nicotinic acid and derivs. and azetidine sterol absorption inhibitor(s) for treatment of vascular indications)

L8 ANSWER 15 OF 21 USPATFULL on STN

AB The present invention provides compositions, therapeutic combinations and methods including: (a) at least one of nicotinic acid or derivatives thereof; and (b) at least one substituted azetidinone or substituted .beta.-lactam sterol absorption inhibitor which can be useful for treating vascular conditions, diabetes, obesity and lowering plasma levels of sterols.

AN 2002:323139 USPATFULL

TI Combinations of nicotinic acid and derivatives thereof and sterol absorption inhibitor(s) and treatments for vascular indications

IN Davis, Harry R., Berkeley Heights, NJ, UNITED STATES
Kosoglou, Teddy, Jamison, PA, UNITED STATES

PA Schering Corporation (U.S. corporation)

PI US 2002183305 A1 20021205

AI US 2002-57646 A1 20020125 (10)

PRAI US 2001-264275P 20010126 (60)
US 2001-323842P 20010921 (60)

DT Utility

FS APPLICATION

LREP SCHERING-PLOUGH CORPORATION, PATENT DEPARTMENT (K-6-1, 1990), 2000 GALLOPING HILL ROAD, KENILWORTH, NJ, 07033-0530

CLMN Number of Claims: 81

ECL Exemplary Claim: 1

DRWN No Drawings

LN.CNT 4256

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

SUMM . . . halting of progression of one or more conditions, for example vascular conditions, such as hyperlipidemia (for example atherosclerosis, hypercholesterolemia or **sitosterolemia**), vascular inflammation, stroke, diabetes, obesity and/or to reduce the level of sterol(s) (such as cholesterol) in the plasma.

SUMM . . . inhibitor(s), to prevent or treat a condition, for example a vascular condition, such as hyperlipidaemia (for example atherosclerosis, hypercholesterolemia or **sitosterolemia**), stroke, diabetes, obesity and/or reduce the level of sterol(s) in the plasma. As used herein, "vascular" comprises cardiovascular, cerebrovascular and. . .

SUMM [0262] In a preferred embodiment, a sterol inhibitor of Formula (I) (**ezetimibe**) useful in the compositions, therapeutic combinations and methods of the present invention is represented by Formula (II) below: ##STR31##

SUMM . . . in a therapeutically effective amount to treat vascular conditions such as atherosclerosis, hyperlipidaemia (including but not limited to hypercholesterolaemia, hypertriglyceridaemia, **sitosterolemia**), stroke, diabetes, obesity, and/or reduce the level of sterol(s) in the plasma. The compositions and treatments can be administered by. . .

DETD . . . cholesterol in mammals, and can be useful in the treatment and/or prevention of vascular conditions, such as atherosclerosis, hypercholesterolemia and **sitosterolemia**, diabetes, obesity and lowering of plasma levels of cholesterol in mammals, in particular in mammals.

IT **163222-33-1P**
(combinations of nicotinic acid and derivs. and azetidine sterol absorption inhibitor(s) for treatment of vascular indications)

L8 ANSWER 16 OF 21 USPATFULL on STN

AB The present invention is directed to the use of sterol absorption inhibiting compounds, pharmaceutical compositions thereof, therapeutic combinations and their use in combination with other lipid lowering agents to treat or prevent **sitosterolemia** and/or to lower the concentration of sterol(s) other than cholesterol in plasma or tissue of a mammal. Methods of treating or preventing vascular disease and coronary events also are provided.

AN 2002:301589 USPATFULL

TI Use of substituted azetidinone compounds for the treatment of **sitosterolemia**

IN Davis, Harry R., Berkeley Heights, NJ, UNITED STATES

PA Schering Corporation (U.S. corporation)

PI US 2002169134 A1 20021114

AI US 2002-57629 A1 20020125 (10)

PRAI US 2001-264645P 20010126 (60)

DT Utility

FS APPLICATION

LREP SCHERING-PLOUGH CORPORATION, PATENT DEPARTMENT (K-6-1, 1990), 2000 GALLOPING HILL ROAD, KENILWORTH, NJ, 07033-0530

CLMN Number of Claims: 58

ECL Exemplary Claim: 1

DRWN No Drawings

LN.CNT 3321

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

TI Use of substituted azetidinone compounds for the treatment of **sitosterolemia**

AB . . . compounds, pharmaceutical compositions thereof, therapeutic combinations and their use in combination with other lipid lowering agents to treat or prevent **sitosterolemia** and/or to lower the concentration of sterol(s) other than cholesterol in plasma or tissue of a mammal. Methods of treating. . .

SUMM [0002] The present invention provides methods and pharmaceutical compositions for treating or preventing **sitosterolemia** by administering to a mammal in need of such treatment an effective amount of at least one treatment composition comprising. . .

SUMM [0003] **Sitosterolemia** is a genetic lipid storage disorder characterized by increased levels of sitosterol and other plant sterols in the plasma and other tissues due to increased non-selective intestinal absorption of sterols and decreased hepatic removal. Individuals having **sitosterolemia** can exhibit one or more of the following conditions: tendon and tuberous xanthomas, arthritis, hemolytic episodes, accelerated atherosclerosis and myocardial. . . can die at an early age due to extensive coronary atherosclerosis. See Nguyen et al., "Regulation of cholesterol biosynthesis in **sitosterolemia**: effects of lovastatin, cholestyramine, and dietary sterol restriction", Vol 32, Journal of Lipid Research, pp. 1941-1948, (1991), incorporated by reference. . .

SUMM [0004] **Sitosterolemia** can be treated with bile acid

sequestrants (such as cholestyramine, colesevelam hydrochloride and colestipol), however, these compounds have a tendency. . .

SUMM [0006] An improved treatment for **sitosterolemia** is needed which can reduce the concentration of sterols in plasma and tissues and inhibit associated debilitating physical effects. Also,. . .

SUMM [0007] The present invention provides a method of treating or preventing **sitosterolemia**, comprising administering to a mammal in need of such treatment an effective amount of at least one sterol absorption inhibitor,. . .

SUMM [0008] In another embodiment, the present invention provides a method of treating or preventing **sitosterolemia**, comprising administering to a mammal in need of such treatment: (1) an effective amount of at least one sterol absorption. . .

SUMM [0009] In another embodiment, the present invention provides a method of treating or preventing **sitosterolemia** comprising administering to a mammal in need of such treatment: (1) an effective amount of at least one sterol absorption. . .

SUMM [0010] Other embodiments of the present invention include pharmaceutical compositions for the treatment or prevention of **sitosterolemia** comprising an effective amount of the compositions or combinations used in the methods described above in a pharmaceutically acceptable carrier.

SUMM [0017] The present invention provides methods, pharmaceutical compositions and combinations for treating or preventing **sitosterolemia** and conditions or symptoms associated with **sitosterolemia** such as are discussed above. Another aspect of the present invention provides methods, pharmaceutical compositions and combinations for reducing the. . . be useful in the treatment and/or prevention of vascular conditions or disease, such as vascular inflammation, arteriosclerosis, atherosclerosis, hypercholesterolemia and **sitosterolemia**, and cardiovascular events, stroke and/or obesity.

SUMM . . . inhibitor of Formula (VII) useful in the compositions, combinations and methods of the present invention is represented by Formula (VII) (**ezetimibe**) below: ##STR42##

SUMM . . . referred to herein as carrier materials). Because of their sterol absorption inhibitory activity, such pharmaceutical compositions possess utility in treating **sitosterolemia** and related disorders.

SUMM . . . can be administered to a mammal in need of such treatment in a pharmaceutically or therapeutically effective amount to treat **sitosterolemia** and/or reduce the level of sterol(s) in the plasma and tissues.

SUMM . . . therapeutic agents, such as sterol absorption inhibitor(s) and bile acid sequestrant(s) or other therapeutic vascular agents, to prevent or treat **sitosterolemia** and/or reduce the level of sterol(s) in the plasma and tissues. As used herein, "vascular" comprises cardiovascular, cerebrovascular and combinations. . .

SUMM . . . the intestinal absorption of sitosterol and can be useful in the treatment and/or prevention of vascular disease, arteriosclerosis, atherosclerosis and **sitosterolemia** in mammals, in particular in humans.

SUMM [0445] In another embodiment, the present invention provides a method of treating or preventing **sitosterolemia** comprising administering to a mammal in need of such treatment an effective amount of at least one sterol absorption inhibitor. . .

SUMM . . . and the second amount taken together in their totality comprise a therapeutically effective amount for the treatment or prevention of **sitosterolemia** in a mammal.

SUMM . . . be useful in the treatment and/or prevention of vascular conditions or disease, such as vascular inflammation, arteriosclerosis, atherosclerosis, hypercholesterolemia and **sitosterolemia**, and cardiovascular events, stroke and obesity.

DETD [0475] In a randomized multicenter, double-blind, placebo-controlled, 8-week trial, 37 human patients previously diagnosed with homozygous

sitosterolemia were randomized to receive Compound VIII (n=30) or placebo (n=7):

DETD . . . T; Kwiterovich, Jr, P O, "Increased sitosterol absorption, decreased removal and expanded body pools compensate for reduced cholesterol synthesis in **sitosterolemia** with xanthomatosis", J Lipid Res, Vol. 30, pp 1319-30, (1989) and Lutjohann, D; Bjorkhem, I; Beil, U F, and von. . .

CLM What is claimed is:

1. A method of treating or preventing **sitosterolemia**, comprising administering to a mammal in need of such treatment an effective amount of at least one sterol absorption inhibitor,. . .

24. A method of treating or preventing **sitosterolemia** comprising administering to a mammal in need of such treatment: (a) an effective amount of a sterol absorption inhibitor represented. . .

25. A pharmaceutical composition for the treatment or prevention of **sitosterolemia**, comprising an effective amount of the sterol absorption inhibitor used in the method of claim 1 in a pharmaceutically acceptable. . .

26. A pharmaceutical composition for the treatment or prevention of **sitosterolemia**, comprising an effective amount of the sterol absorption inhibitor used in the method of claim 8 in a pharmaceutically acceptable. . .

27. A pharmaceutical composition for the treatment or prevention of **sitosterolemia**, comprising an effective amount of the compound of Formula (VIII) ##STR91## in a pharmaceutically acceptable carrier.

28. A pharmaceutical composition for the treatment or prevention of **sitosterolemia**, comprising: a) an effective amount of the compound of Formula (VIII) ##STR92## and b) an effective amount of a lipid. . .

32. A method of treating or preventing **sitosterolemia**, comprising administering to a mammal in need of such treatment: (1) an effective amount of at least one sterol absorption. . .

33. A method of treating or preventing **sitosterolemia** comprising administering to a mammal in need of such treatment: (1) an effective amount of at least one sterol absorption. . .

46. A pharmaceutical composition for the treatment or prevention of **sitosterolemia**, comprising: a) an effective amount of the compound of Formula (VIII) ##STR95## and b) an effective amount of a bile. . .

. . . wherein the first amount and the second amount together comprise a therapeutically effective amount for the treatment or prevention of **sitosterolemia** in a mammal.

. . . wherein the first amount and the second amount together comprise a therapeutically effective amount for the treatment or prevention of **sitosterolemia** in a mammal.

IT **163222-33-1P**
(azetidinone derivs. for treatment of sitosterolemia)

IT 11041-12-6, Cholestyramine 50925-79-6, Colestipol 75330-75-5, Lovastatin 79902-63-9, Simvastatin 81093-37-0, Pravastatin 93957-54-1, Fluvastatin 134523-00-5, Atorvastatin 147511-69-1, Itavastatin **163222-33-1D**, prodrug derivs. 182815-44-7, Colesevelam hydrochloride 287714-41-4, Rosuvastatin 438576-91-1 438576-91-1D, derivs. 438576-92-2 438576-92-2D, prodrug derivs. 444313-49-9 444313-50-2 444313-51-3 444313-53-5 444313-55-7 444313-57-9 444313-59-1 444313-60-4 444313-61-5 444313-62-6
(azetidinone derivs. for treatment of sitosterolemia)

L8 ANSWER 17 OF 21 USPATFULL on STN

AB The present invention provides compositions, therapeutic combinations and methods including: (a) at least one peroxisome proliferator-activated receptor activator; and (b) at least one substituted

azetidinone or substituted .beta.-lactam sterol absorption inhibitor which can be useful for treating vascular conditions, diabetes, obesity and lowering plasma levels of sterols.

AN 2002:273408 USPATFULL

TI Combinations of peroxisome proliferator-activated receptor (PPAR) activator(s) and sterol absorption inhibitor(s) and treatments for vascular indications

IN Davis, Harry R., Berkeley Heights, NJ, UNITED STATES
Kosoglou, Teddy, Jamison, PA, UNITED STATES
Picard, Gilles J., Brussels, BELGIUM

PA Schering Corporation (U.S. corporation)

PI US 2002151536 A1 20021017

AI US 2002-57323 A1 20020125 (10)

PRAI US 2001-264396P 20010126 (60)
US 2001-323839P 20010921 (60)

DT Utility

FS APPLICATION

LREP SCHERING-PLOUGH CORPORATION, PATENT DEPARTMENT (K-6-1, 1990), 2000 GALLOPING HILL ROAD, KENILWORTH, NJ, 07033-0530

CLMN Number of Claims: 101

ECL Exemplary Claim: 1

DRWN No Drawings

LN.CNT 5004

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

SUMM . . . halting of progression of one or more conditions, for example vascular conditions, such as hyperlipidaemia (for example atherosclerosis, hypercholesterolemia or **sitosterolemia**), vascular inflammation, stroke, diabetes, obesity and/or to reduce-the level of sterol(s) (such as cholesterol) in the plasma.

SUMM . . . inhibitor(s), to prevent or treat a condition, for example a vascular condition, such as hyperlipidaemia (for example atherosclerosis, hypercholesterolemia or **sitosterolemia**), vascular inflammation, stroke, diabetes, obesity and/or reduce the level of sterol(s) (such as cholesterol) in the plasma. As used herein,. . .

SUMM . . . of Formula (I) useful in the compositions, therapeutic combinations and methods of the present invention is represented by Formula (II) (**ezetimibe**) below: ##STR33##

SUMM . . . treat one or more conditions, for example vascular conditions such as atherosclerosis, hyperlipidaemia (including but not limited to hypercholesterolemia, hypertriglyceridaemia, **sitosterolemia**), vascular inflammation, stroke, diabetes, obesity, and/or reduce the level of sterol(s) in the plasma. The compositions and treatments can be. . .

DETD . . . and can be useful in the treatment and/or prevention of conditions, for example vascular conditions, such as atherosclerosis, hypercholesterolemia and **sitosterolemia**, stroke, obesity and lowering of plasma levels of cholesterol in mammals, in particular in mammals.

IT **163222-33-1P**
(combinations of nicotinic acid and derivs. and azetidine sterol absorption inhibitor(s) for treatment of vascular indications)

L8 ANSWER 18 OF 21 USPATFULL on STN

AB The present invention provides compositions, therapeutic combinations and methods including: (a) at least one sterol absorption inhibitor; and (b) at least one blood modifier, which can be useful for treating vascular conditions and lowering plasma levels of sterols.

AN 2002:266305 USPATFULL

TI Combinations of sterol absorption inhibitor(s) with blood modifier(s) for treating vascular conditions

IN Kosoglou, Teddy, Jamison, PA, UNITED STATES
Ress, Rudyard J., Flemington, NJ, UNITED STATES
Strony, John T., Lebanon, NJ, UNITED STATES
Veltri, Enrico P., Princeton, NJ, UNITED STATES

PA Schering Corporation (U.S. corporation)
PI US 2002147184 A1 20021010
AI US 2002-56680 A1 20020125 (10)
PRAI US 2001-324123P 20010921 (60)
US 2001-264396P 20010126 (60)
US 2001-264600P 20010126 (60)
US 2001-264275P 20010126 (60)
DT Utility
FS APPLICATION
LREP SCHERING-PLOUGH CORPORATION, PATENT DEPARTMENT (K-6-1, 1990), 2000 GALLOPING HILL ROAD, KENILWORTH, NJ, 07033-0530
CLMN Number of Claims: 48
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 3296
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
DETD . . . in a therapeutically effective amount to treat "vascular conditions" such as atherosclerosis, hyperlipidaemia (including but not limited to hypercholesterolaemia, hypertriglyceridaemia, **sitosterolemia**), vascular inflammation, hypertension, angina, cardiac arrhythmias, stroke, as well as conditions such diabetes, obesity, and/or to reduce the level of. . .
DETD . . . of Formula (I) useful in the compositions, therapeutic combinations and methods of the present invention is represented by Formula (II) (**ezetimibe**) below: ##STR3##
DETD . . . mammals, and can be useful in the treatment and/or prevention of vascular conditions, such as vascular inflammation, atherosclerosis, hypercholesterolemia and **sitosterolemia**, stroke, vascular conditions and lowering of plasma levels of cholesterol in mammals, in particular in humans.
IT **163222-33-1P**
(combinations of nicotinic acid and derivs. and azetidine sterol absorption inhibitor(s) for treatment of vascular indications)

L8 ANSWER 19 OF 21 CAPLUS COPYRIGHT 2003 ACS on STN DUPLICATE 3
AB The review on clin. trials establishing the efficacy and safety of **ezetimibe** 10 mg once daily, as monotherapy and co-administered with statins, for the treatment of hypercholesterolemia. As monotherapy, **ezetimibe** produced redns. in low-d. lipoprotein cholesterol (LDL-C) of approx. 18% ($P < 0.01$ compared with placebo). As add-on therapy for patients who failed to meet target redns. with statin monotherapy, the addn. of **ezetimibe** produced a 21.4% addnl. redn. in LDL-C compared with statin monotherapy ($P < 0.001$). Addn. of **ezetimibe** to statin therapy also significantly improved high-d. lipoprotein cholesterol and triglyceride levels compared with statin monotherapy ($P < 0.05$, $P < 0.001$, resp.). In four studies in which **ezetimibe** 10 mg was co-administered with simvastatin, atorvastatin, pravastatin, or lovastatin at different dosages, redns. in LDL-C levels with co-administration were significantly greater than those obtained with the corresponding statin monotherapy dose. **Ezetimibe** plus 10 mg of simvastatin or atorvastatin produced LDL-C redns. comparable to 80 mg of the resp. statin monotherapy. In all the clin. trials, **ezetimibe** was well tolerated, with a safety profile comparable to that of statin monotherapy and to that of placebo. Drug-drug interactions have not been obsd. when **ezetimibe** is given concomitantly with statins, fenofibrate, oral contraceptives, or a no. of other commonly administered drugs. In the phase II and phase III clin. trial development program, **ezetimibe** has been shown to be an effective and safe new option for treating hypercholesterolemia even in difficult-to-treat populations such as homozygous and heterozygous familial hypercholesterolemia and **sitosterolemia**.
AN 2003:30938 CAPLUS
DN 138:66084
TI **Ezetimibe**: efficacy and safety in clinical trials

AU Ballantyne, C. M.
CS Center for Cardiovascular Disease Prevention, Methodist DeBakey Heart Center, Baylor College of Medicine, TX, USA
SO European Heart Journal Supplements (2002), 4(Suppl. J), J9-J18
CODEN: EHJSFT; ISSN: 1520-765X
PB W. B. Saunders
DT Journal; General Review
LA English
RE.CNT 34 THERE ARE 34 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT
TI **Ezetimibe**: efficacy and safety in clinical trials
AB The review on clin. trials establishing the efficacy and safety of **ezetimibe** 10 mg once daily, as monotherapy and co-administered with statins, for the treatment of hypercholesterolemia. As monotherapy, **ezetimibe** produced redns. in low-d. lipoprotein cholesterol (LDL-C) of approx. 18% ($P < 0.01$ compared with placebo). As add-on therapy for patients who failed to meet target redns. with statin monotherapy, the addn. of **ezetimibe** produced a 21.4% addnl. redn. in LDL-C compared with statin monotherapy ($P < 0.001$). Addn. of **ezetimibe** to statin therapy also significantly improved high-d. lipoprotein cholesterol and triglyceride levels compared with statin monotherapy ($P < 0.05$, $P < 0.001$, resp.). In four studies in which **ezetimibe** 10 mg was co-administered with simvastatin, atorvastatin, pravastatin, or lovastatin at different dosages, redns. in LDL-C levels with co-administration were significantly greater than those obtained with the corresponding statin monotherapy dose. **Ezetimibe** plus 10 mg of simvastatin or atorvastatin produced LDL-C redns. comparable to 80 mg of the resp. statin monotherapy. In all the clin. trials, **ezetimibe** was well tolerated, with a safety profile comparable to that of statin monotherapy and to that of placebo. Drug-drug interactions have not been obsd. when **ezetimibe** is given concomitantly with statins, fenofibrate, oral contraceptives, or a no. of other commonly administered drugs. In the phase II and phase III clin. trial development program, **ezetimibe** has been shown to be an effective and safe new option for treating hypercholesterolemia even in difficult-to-treat populations such as homozygous and heterozygous familial hypercholesterolemia and **sitosterolemia**.
ST review **ezetimibe** hypocholesteremic statin synergistic cholesterol absorption hypercholesterolemia
IT Anticholesteremic agents
Human
Hypercholesterolemia
(**ezetimibe** for treatment of hyperlipidemia)
IT Glycerides, biological studies
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(**ezetimibe** for treatment of hyperlipidemia)
IT Lipids, biological studies
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(hyperlipidemia; **ezetimibe** for treatment of hyperlipidemia)
IT Lipoproteins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(low-d., blood; **ezetimibe** for treatment of hyperlipidemia)
IT Drug interactions
(synergistic; **ezetimibe** for treatment of hyperlipidemia)
IT Biological transport
(uptake; **ezetimibe** for treatment of hyperlipidemia)
IT **163222-33-1**, **Ezetimibe**
RL: ADV (Adverse effect, including toxicity); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**ezetimibe** for treatment of hyperlipidemia)
IT 57-88-5, Cholesterol, biological studies
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(**ezetimibe** for treatment of hyperlipidemia)
IT 9028-35-7

RL: BSU (Biological study, unclassified); BIOL (Biological study) (inhibitors, statins; **ezetimibe** for treatment of hyperlipidemia)

L8 ANSWER 20 OF 21 CAPLUS COPYRIGHT 2003 ACS on STN

AB A review. Serum cholesterol levels are normally maintained within narrow limits. This is accomplished by the integrated actions of several homeostatic mechanisms. These include: cholesterol absorption, cholesterol synthesis, cholesterol transport, lipoprotein receptor mediated tissue uptake of cholesterol, degrdn. of cholesterol to bile acids, and elimination of cholesterol from the body. Impairment in any of these processes can lead to alterations in serum levels and result in significant pathol. Thus, many investigators have sought to understand the mol. basis of these homeostatic processes. Our own work has centered mainly on hepatic cholesterol synthesis, bile acid synthesis, and the LDL receptor. In this review we aim to present recent advances in our understanding of these homeostatic processes. Recent studies have demonstrated that there is considerable variation among individuals with respect to the amt. of cholesterol that they absorb. The role of the ATP binding cassette proteins, ABCG5 and ABCG8, in cholesterol efflux from the intestine has been established. A mutation in either of these proteins causes **sitosterolemia**, which results in increased absorption of cholesterol and plant sterols and reduced excretion of sterols into the bile. **Ezetimibe**, a selective inhibitor of intestinal absorption of cholesterol, is now in phase III studies. An inverse relationship between cholesterol absorption and cholesterol synthesis has been established. The mechanism by which dietary cholesterol feeds back to regulate hepatic cholesterol biosynthesis by down regulating the expression of HMG-CoA reductase appears to normally involve translational control. The possible participation of oxylanosterols in this regulation has been suggested. A pos. correlation between the rate of cholesterol synthesis and response to effective cholesterol lowering by statin treatment has been established. A role for hepatic HMG-CoA reductase in buffering against the serum cholesterol raising action of dietary cholesterol has been demonstrated in inbred rats, hamsters, and hormone-deficient animals. The hepatic LDL receptor is markedly and rapidly induced by thyroid hormone. It appears that hepatic cholesterol levels may affect LDL receptor activity by altering the rate of cycling of the receptor rather than the steady state level. In liver, a substantial portion of LDL receptors is located in caveolae and assocd. with caveolin-1. A cytosolic protein that contains a phosphotyrosine-binding domain, which is defective in autosomal recessive hypercholesterolemia, also may bind to the LDL receptor and modulate receptor function in liver but not in fibroblasts. This protein may serve as a LDL receptor adaptor protein. Mutations in either apo B or apo E, ligands for the LDL receptor, result in elevated serum cholesterol levels. The thyroid hormone increases the expression of apo A-I leading to higher HDL levels and enhanced reverse cholesterol transport. The HDL receptor located in adrenal, ovary, testes, and liver transfers cholesterol from HDL into cells by transcytosis. Increased expression of cholesterol 7.alpha. hydroxylase lowers serum cholesterol levels even in LDL receptor neg. mice.

AN 2003:285911 CAPLUS

DN 139:50179

TI Cholesterol homeostasis

AU Ness, Gene C.

CS Department of Biochemistry and Molecular Biology, College of Medicine, University of South Florida, Tampa, FL, 33612, USA

SO Sterols and Oxysterols (2002), 1-14. Editor(s): Fliesler, Steven J. Publisher: Research Signpost, Trivandrum, India. CODEN: 69DTPM; ISBN: 81-7736-069-8

DT Conference; General Review

LA English

RE.CNT 82 THERE ARE 82 CITED REFERENCES AVAILABLE FOR THIS RECORD

ALL CITATIONS AVAILABLE IN THE RE FORMAT

AB A review. Serum cholesterol levels are normally maintained within narrow limits. This is accomplished by the integrated actions of several homeostatic mechanisms. These include: cholesterol absorption, cholesterol synthesis, cholesterol transport, lipoprotein receptor mediated tissue uptake of cholesterol, degrdn. of cholesterol to bile acids, and elimination of cholesterol from the body. Impairment in any of these processes can lead to alterations in serum levels and result in significant pathol. Thus, many investigators have sought to understand the mol. basis of these homeostatic processes. Our own work has centered mainly on hepatic cholesterol synthesis, bile acid synthesis, and the LDL receptor. In this review we aim to present recent advances in our understanding of these homeostatic processes. Recent studies have demonstrated that there is considerable variation among individuals with respect to the amt. of cholesterol that they absorb. The role of the ATP binding cassette proteins, ABCG5 and ABCG8, in cholesterol efflux from the intestine has been established. A mutation in either of these proteins causes **sitosterolemia**, which results in increased absorption of cholesterol and plant sterols and reduced excretion of sterols into the bile. **Ezetimibe**, a selective inhibitor of intestinal absorption of cholesterol, is now in phase III studies. An inverse relationship between cholesterol absorption and cholesterol synthesis has been established. The mechanism by which dietary cholesterol feeds back to regulate hepatic cholesterol biosynthesis by down regulating the expression of HMG-CoA reductase appears to normally involve translational control. The possible participation of oxylanosterols in this regulation has been suggested. A pos. correlation between the rate of cholesterol synthesis and response to effective cholesterol lowering by statin treatment has been established. A role for hepatic HMG-CoA reductase in buffering against the serum cholesterol raising action of dietary cholesterol has been demonstrated in inbred rats, hamsters, and hormone-deficient animals. The hepatic LDL receptor is markedly and rapidly induced by thyroid hormone. It appears that hepatic cholesterol levels may affect LDL receptor activity by altering the rate of cycling of the receptor rather than the steady state level. In liver, a substantial portion of LDL receptors is located in caveolae and assocd. with caveolin-1. A cytosolic protein that contains a phosphotyrosine-binding domain, which is defective in autosomal recessive hypercholesterolemia, also may bind to the LDL receptor and modulate receptor function in liver but not in fibroblasts. This protein may serve as a LDL receptor adaptor protein. Mutations in either apo B or apo E, ligands for the LDL receptor, result in elevated serum cholesterol levels. The thyroid hormone increases the expression of apo A-I leading to higher HDL levels and enhanced reverse cholesterol transport. The HDL receptor located in adrenal, ovary, testes, and liver transfers cholesterol from HDL into cells by transcytosis. Increased expression of cholesterol 7.alpha. hydroxylase lowers serum cholesterol levels even in LDL receptor neg. mice.

L8 ANSWER 21 OF 21 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN
AN 2003:79148 BIOSIS
DN PREV200300079148
TI **Ezetimibe** is an effective treatment for homozygous **sitosterolemia**.
AU Salen, Gerald (1); von Bergmann, Klaus; Kwiterovich, Peter; Musser, Bret; O'Grady, Laura; Stein, Peter; Musliner, Thomas
CS (1) Univ of Medicine and Dentistry of New Jersey, Newark, NJ, USA USA
SO Circulation, (November 5 2002) Vol. 106, No. 19 Supplement, pp. II-185. print.
Meeting Info.: Abstracts from Scientific Sessions Chicago, IL, USA November 17-20, 2002 American Heart Association
. ISSN: 0009-7322.
DT Conference
LA English

TI **Ezetimibe** is an effective treatment for homozygous **sitosterolemia**.
IT . . . Concepts
Cardiovascular Medicine (Human Medicine, Medical Sciences); Medical Genetics (Allied Medical Sciences); Pharmacology
IT Diseases
atherosclerosis: genetics, vascular disease; homozygous **sitosterolemia**: genetic disease
IT Chemicals & Biochemicals
Apo B [apolipoprotein B]; LDL-C [low-density lipoprotein cholesterol]; bile salt binding resin; campesterol: absorption, excretion; cholesterol; **ezetimibe**: metabolic - drug; plant sterols: absorption, excretion; sitosterol: absorption, excretion
IT Alternate Indexing
Arteriosclerosis (MeSH)
RN 474-62-4 (CAMPESTEROL)
57-88-5 (CHOLESTEROL)
163222-33-1 (**EZETIMIBE**)

=>
=> s l5 and sitosterolemia
L9 24 L5 AND SITOSTEROLEMIA

=> dup rem l9
PROCESSING COMPLETED FOR L9
L10 19 DUP REM L9 (5 DUPLICATES REMOVED)

=> d l10 1-19 ab bib kwic

L10 ANSWER 1 OF 19 USPATFULL on STN
AB The present invention provides therapeutic combinations and methods including at least one sterol or 5.alpha.-stanol absorption inhibitor that can be useful for treating xanthomas.
AN 2003:173961 USPATFULL
TI Methods and therapeutic combinations for the treatment of xanthoma using sterol absorption inhibitors
IN Davis, Harry R., Berkeley Heights, NJ, UNITED STATES
PA Schering Corporation (U.S. corporation)
PI US 2003119809 A1 20030626
AI US 2002-247095 A1 20020919 (10)
PRAI US 2001-323942P 20010921 (60)
DT Utility
FS APPLICATION
LREP SCHERING-PLOUGH CORPORATION, PATENT DEPARTMENT (K-6-1, 1990), 2000 GALLOPING HILL ROAD, KENILWORTH, NJ, 07033-0530
CLMN Number of Claims: 23
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 2722
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
SUMM . . . MEVACOR.RTM. which is available from Merck & Co.), pravastatin (for example PRAVACHOL.RTM. which is available from Bristol Meyers Squibb), fluvastatin, **simvastatin** (for example ZOCOR.RTM. which is available from Merck & Co.), atorvastatin, cerivastatin, CI-981, rivastatin (sodium 7-(4-fluorophenyl)-2,6-diisopropyl-5-methoxymethylpyridin-3-yl)-3,5-dihydroxy-6-heptanoate), rosuvastatin and pitavastatin. . . NB-598 ((E)-N-ethyl-N-(6,6-dimethyl-2-hepten-4-ynyl)-3-[(3,3'-bithiophen-5-yl)methoxy]benzene-methanamine hydrochloride) and other sterol biosynthesis inhibitors such as DMP-565. Preferred HMG CoA reductase inhibitors include lovastatin, pravastatin and **simvastatin**. The most preferred HMG CoA reductase inhibitor is **simvastatin**.
DETD . . . cholesterol in mammals, and can be useful in the treatment

and/or prevention of vascular conditions, such as atherosclerosis, hypercholesterolemia and **sitosterolemia**, vascular inflammation, stroke, obesity and lowering of plasma levels of cholesterol in subjects, in particular in humans. As used herein,. . .

CLM What is claimed:

. . . The method according to claim 13, wherein the HMG-CoA reductase inhibitor is selected from the group consisting of pravastatin, lovastatin, **simvastatin**, fluvastatin, rivastatin, rosuvastatin, atorvastatin, cerivastatin, and combinations thereof.

IT 59-67-6, Nicotinic acid, biological studies 59-67-6D, Nicotinic acid, derivs. 23288-49-5, Probucol 23288-49-5D, Probucol, derivs. 55121-56-7D, Azetidinone, derivs. 75330-75-5, Lovastatin **79902-63-9**, Simvastatin 81093-37-0, Pravastatin 93957-54-1, Fluvastatin 134523-00-5, Atorvastatin 143201-11-0, Rivastatin 145599-86-6, Cerivastatin 287714-41-4, Rosuvastatin
(sterol/5.alpha.-stanol absorption inhibitors for treatment of xanthoma, and use with other agents)

L10 ANSWER 2 OF 19 USPATFULL on STN

AB The present invention relates to methods of treating or preventing cardiovascular conditions while preventing or minimizing muscular degeneration side effects associated with certain HMG-CoA reductase inhibitors by coadministration of at least one sterol or 5.alpha.-stanol absorption inhibitor, pharmaceutically acceptable salts or solvates thereof, and at least one HMG-CoA reductase inhibitor, the latter being used sparingly in amounts insufficient to cause muscle degeneration.

AN 2003:173960 USPATFULL

TI Methods of treating or preventing cardiovascular conditions while preventing or minimizing muscular degeneration side effects

IN LeBeaut, Alexandre P., Morristown, NJ, UNITED STATES
Davis, Harry R., Berkeley Heights, NJ, UNITED STATES

PA Schering Corporation (U.S. corporation)

PI US 2003119808 A1 20030626

AI US 2002-246996 A1 20020919 (10)

PRAI US 2001-324121P 20010921 (60)
US 2002-351957P 20020125 (60)

DT Utility

FS APPLICATION

LREP SCHERING-PLOUGH CORPORATION, PATENT DEPARTMENT (K-6-1, 1990), 2000 GALLOPING HILL ROAD, KENILWORTH, NJ, 07033-0530

CLMN Number of Claims: 23

ECL Exemplary Claim: 1

DRWN No Drawings

LN.CNT 3092

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

SUMM . . . MEVACOR.RTM. which is available from Merck & Co.), pravastatin (for example PRAVACHOL.RTM. which is available from Bristol Meyers Squibb), fluvastatin, **simvastatin** (for example ZOCOR.RTM. which is available from Merck & Co.), atorvastatin, [cerivastatin] withdrawn from the market, CI-981, rivastatin (sodium 7-(4-fluorophenyl)-2,6-diisopropyl-5-methoxymethylpyridin-3-yl)-3,5-dihydroxy-6-heptanoate). . . pitavastatin (such as NK-104 of Negma Kowa of Japan). Preferred HMG CoA reductase inhibitors include lovastatin, pravastatin , atorvastatin and **simvastatin**. The most preferred HMG CoA reductase inhibitors are **simvastatin** and atorvastatin.

SUMM . . . with the at least one sterol or 5.alpha.-stanol absorption inhibitor, e.g.;

HMG CoA Reductase Inhibitor	Approved Dose (mg)
simvastatin	5, 10, 20, 40, 80

pravastatin 10, 20, 40
atorvastatin 10, 20, 40, 80
lovastatin 10, 20, 40

SUMM . . . can further be used to treat or prevent vascular disease or conditions (such as for example atherosclerosis, arteriosclerosis, hypercholesterolemia and/or **sitosterolemia**), cardiovascular events, hypertension, obesity, stroke, lowering of a concentration of a sterol in plasma of a mammal, reducing vascular inflammation. . .

SUMM . . . the above-described tablet can be coadministered with a tablet, capsule, etc. comprising a dosage of Active Compound II, for example **simvastatin** as described above.

SUMM . . . 5.alpha.-stanols in subjects and can be useful in the treatment and/or prevention of vascular conditions, such as atherosclerosis, hypercholesterolemia and **sitosterolemia**, stroke, obesity and lowering of plasma levels of sterols such as cholesterol or 5.alpha.-stanols in subject, in particular in humans.

CLM What is claimed:

. . . 1, wherein the at least one HMG-CoA reductase inhibitor is selected from the group consisting of lovastatin, pravastatin, rivastatin, fluvastatin, **simvastatin**, atorvastatin, cerivastatin and combinations thereof.

15. The method of claim 1, wherein the at least one HMG-CoA reductase inhibitor is **simvastatin**.

IT 75330-75-5, Lovastatin **79902-63-9**, Simvastatin 81093-37-0, Pravastatin 93957-54-1, Fluvastatin 134523-00-5, Atorvastatin 143201-11-0, Rivastatin 145599-86-6, Cerivastatin
(HMG-CoA reductase inhibitor; sterol or 5.alpha.-stanol absorption inhibitor and HMG-CoA reductase inhibitor for treating or preventing cardiovascular conditions while preventing muscle degeneration side effects)

L10 ANSWER 3 OF 19 USPATFULL on STN

AB The present invention provides compositions, therapeutic combinations and methods including: (a) at least one hormone replacement therapy composition; and (b) at least one sterol absorption inhibitor which can be useful for treating vascular conditions in post-menopausal women and lowering plasma levels of sterols or 5.alpha.-stanols.

AN 2003:173948 USPATFULL

TI Combinations of hormone replacement therapy composition(s) and sterol absorption inhibitor(s) and treatments for vascular conditions in post-menopausal women

IN Strony, John T., Lebanon, NJ, UNITED STATES

PA Schering Corporation (U.S. corporation)

PI US 2003119796 A1 20030626

AI US 2002-247085 A1 20020919 (10)

RLI Continuation-in-part of Ser. No. US 2002-166942, filed on 11 Jun 2002, PENDING

PRAI US 2001-324118P 20010921 (60)

DT Utility

FS APPLICATION

LREP SCHERING-PLOUGH CORPORATION, PATENT DEPARTMENT (K-6-1, 1990), 2000 GALLOPING HILL ROAD, KENILWORTH, NJ, 07033-0530

CLMN Number of Claims: 44

ECL Exemplary Claim: 1

DRWN No Drawings

LN.CNT 2932

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

SUMM . . . or halting of progression of the condition, for example a vascular condition, such as hyperlipidaemia (for example atherosclerosis, hypercholesterolemia or **sitosterolemia**), vascular inflammation, stroke, diabetes, obesity and/or reduce the level of sterol(s) (such as cholesterol) in the plasma of a patient,. . .

SUMM . . . MEVACOR.RTM. which is available from Merck & Co.), pravastatin (for example PRAVACHOL.RTM. which is available from Bristol Meyers Squibb), fluvastatin, **simvastatin** (for example ZOCOR.RTM. which is available from Merck & Co.), atorvastatin, cerivastatin, CI-981, rivastatin (sodium 7-(4-fluorophenyl)-2,6-diisopropyl-5-methoxymethylpyridin-3-yl)-3,5-dihydroxy-6-heptanoate) and pitavastatin (such as. . . NB-598 ((E)-N-ethyl-N-(6,6-dimethyl-2-hepten-4-ynyl)-3-[(3,3'-bithiophen-5-yl)methoxy]benzene-methanamine hydrochloride) and other sterol biosynthesis inhibitors such as DMP-565. Preferred HMG CoA reductase inhibitors include lovastatin, pravastatin and **simvastatin**. The most preferred HMG CoA reductase inhibitor is **simvastatin**.

DETD . . . 5.alpha.-stanol in subjects and can be useful in the treatment and/or prevention of vascular conditions, such as atherosclerosis, hypercholesterolemia and **sitosterolemia**, stroke, obesity and lowering of plasma levels of cholesterol in mammals, in particular in humans such as women, and preferably. . .

CLM What is claimed:

. . . 22, wherein the at least one HMG CoA reductase inhibitor is selected from the group consisting of lovastatin, pravastatin, fluvastatin, **simvastatin**, atorvastatin, cerivastatin and mixtures thereof.

24. The composition according to claim 23, wherein the at least one HMG CoA reductase inhibitor is **simvastatin**.

IT 50-28-2, Estradiol, biological studies 57-63-6, Ethinyl estradiol 57-83-0, Pregn-4-ene-3, 20-dione, biological studies 58-18-4, Methyltestosterone 59-67-6, Nicotinic acid, biological studies 68-22-4, Norethindrone 71-58-9, Medroxyprogesterone acetate 72-33-3, Mestranol 297-76-7, Ethynodiol diacetate 438-67-5, Sodium estrone sulfate 520-85-4, Medroxyprogesterone 797-63-7, Levonorgestrel 4999-79-5, 17.beta.-Estradiol sodium sulfate 6533-00-2, Norgestrel 16680-47-0, Sodium equilin sulfate 16680-48-1, Equilenin sodium sulfate 16680-49-2, Sodium 17.beta.-dihydroequilin sulfate 16680-50-5, 17.beta.-Dihydroequilenin sodium sulfate 23288-49-5, Probucol 35189-28-7, Norgestimate 38600-07-6, Sodium 17.alpha.-estradiol sulfate 38600-08-7, Sodium 17.alpha.-dihydroequilenin sulfate 38600-09-8, Sodium 17.alpha.-dihydroequilin sulfate 54024-22-5, Desogestrel 75330-75-5, Lovastatin **79902-63-9**, Simvastatin 81093-37-0, Pravastatin 93957-54-1, Fluvastatin 134523-00-5, Atorvastatin 145599-86-6, Cerivastatin
(combinations of hormone replacement therapy compn.(s) and sterol absorption inhibitor(s) and treatments for vascular conditions in post-menopausal women)

L10 ANSWER 4 OF 19 USPATFULL on STN

AB The present invention provides methods for treating or preventing vascular inflammation or for reducing blood levels of c-reactive protein by administering at least one sterol absorption inhibitor and/or at least one 5.alpha.-stanol absorption inhibitor.

AN 2003:173909 USPATFULL

TI Methods for treating or preventing vascular inflammation using sterol absorption inhibitor(s)

IN Davis, Harry R., Berkeley Heights, NJ, UNITED STATES

PA Schering Corporation (U.S. corporation)

PI US 2003119757 A1 20030626

AI US 2002-247032 A1 20020919 (10)

RLI Continuation-in-part of Ser. No. US 2002-166942, filed on 11 Jun 2002, PENDING

PRAI US 2001-323937P 20010921 (60)

DT Utility

FS APPLICATION

LREP SCHERING-PLOUGH CORPORATION, PATENT DEPARTMENT (K-6-1, 1990), 2000 GALLOPING HILL ROAD, KENILWORTH, NJ, 07033-0530

CLMN Number of Claims: 35
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 3032
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
SUMM . . . MEVACOR.RTM. which is available from Merck & Co.), pravastatin (for example PRAVACHOL.RTM. which is available from Bristol Meyers Squibb), fluvastatin, **simvastatin** (for example ZOCOR.RTM. which is available from Merck & Co.), atorvastatin, cerivastatin, CI-981 and pitavastatin (such as NK-104 of Negma. . . NB-598 ((E)-N-ethyl-N-(6,6-dimethyl-2-hepten-4-ynyl)-3-[(3,3'-bithiophen-5-yl)methoxy]benzene-methanamine hydrochloride) and other sterol biosynthesis inhibitors such as DMP-565. Preferred HMG CoA reductase inhibitors include lovastatin, pravastatin and **simvastatin**. The most preferred HMG CoA reductase inhibitor is **simvastatin**.

SUMM . . . Preferably the cholesterol biosynthesis inhibitor comprises one or more HMG CoA reductase inhibitors, such as, for example, lovastatin, pravastatin and/or **simvastatin**. More preferably, the method comprises the compound of Formula (II) in combination with **simvastatin** and gemfibrozil or fenofibrate.

DETD . . . blood and can be useful in the treatment as well as prevention of vascular conditions, such as atherosclerosis, hypercholesterolemia and **sitosterolemia**, stroke, obesity and lower plasma levels of sterols and/or 5.alpha.-stanols in a subject, in particular in humans, such as phytosterols. . .

DETD . . . 12 consecutive weeks: a tablet formulation as described above having 10 milligrams of the compound of Formula (II) "Composition A"; **SIMVASTATIN** 10, 20, 40 or 80 mg (available from Merck & Co., Inc.); coadministration of Composition A+**SIMVASTATIN** 10, 20, 40 or 80 mg; or placebo.

DETD [0512] Pooled subjects treated with Composition A+**SIMVASTATIN** had reduced LDL-C from baseline by 49.9% vs. pooled subjects treated with **SIMVASTATIN** alone (36.1%, P<0.01) and co-administration of Composition A+**SIMVASTATIN** was superior to statin alone at each **SIMVASTATIN** dose. Overall, median percent reductions in CRP from baseline were almost 2.times.greater with pooled Composition A+**SIMVASTATIN** vs. pooled **SIMVASTATIN** alone (-34.8% vs -18.2%, P<0.01). Median CRP was reduced in pooled Composition A+**SIMVASTATIN** to 0.180 mg/dL and with **SIMVASTATIN** to 0.215 mg/dL (P=0.03). CRP reductions by Composition A+**SIMVASTATIN** were comparable to **SIMVASTATIN** 80.

CLM What is claimed is:
. . . 19, wherein the at least one HMG CoA reductase inhibitor is selected from the group consisting of lovastatin, pravastatin, fluvastatin, **simvastatin**, atorvastatin, cerivastatin and mixtures thereof.

IT 75330-75-5, Lovastatin **79902-63-9**, Simvastatin 81093-37-0, Pravastatin 93957-54-1, Fluvastatin 134523-00-5, Atorvastatin 145599-86-6, Cerivastatin
(HMG-CoA reductase inhibitor; sterol or 5.alpha.-stanol absorption inhibitor for reducing blood levels of C-reactive protein and treating or preventing vascular inflammation)

L10 ANSWER 5 OF 19 USPATFULL on STN
AB The present invention provides methods for the treatment of obesity using sterol or 5.alpha.-stanol absorption inhibitors and compositions and therapeutic combinations including sterol or 5.alpha.-stanol absorption inhibitors and at least one obesity control medication.
AN 2003:173582 USPATFULL
TI Methods and therapeutic combinations for the treatment of obesity using sterol absorption inhibitors
IN Davis, Harry R., Berkeley Heights, NJ, UNITED STATES
Ress, Rudyard J., Flemington, NJ, UNITED STATES
Strony, John T., Lebanon, NJ, UNITED STATES

Veltri, Enrico P., Princeton, NJ, UNITED STATES
PA Schering Corporation (U.S. corporation)
PI US 2003119428 A1 20030626
AI US 2002-247397 A1 20020919 (10)
RLI Continuation-in-part of Ser. No. US 2002-166942, filed on 11 Jun 2002, PENDING
PRAI US 2001-323840P 20010921 (60)
DT Utility
FS APPLICATION
LREP SCHERING-PLOUGH CORPORATION, PATENT DEPARTMENT (K-6-1, 1990), 2000 GALLOPING HILL ROAD, KENILWORTH, NJ, 07033-0530
CLMN Number of Claims: 35
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 3027
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
SUMM . . . MEVACOR.RTM. which is available from Merck & Co.), pravastatin (for example PRAVACHOL.RTM. which is available from Bristol Meyers Squibb), fluvastatin, **simvastatin** (for example ZOCOR.RTM. which is available from Merck & Co.), atorvastatin, cerivastatin, CI-981, rivastatin (sodium 7-(4-fluorophenyl)-2,6-diisopropyl-5-methoxymethylpyridin-3-yl)-3,5-dihydroxy-6-heptanoate) and pitavastatin (such as. . . NB-598 ((E)-N-ethyl-N-(6,6-dimethyl-2-hepten-4-ynyl)-3-[(3,3'-bithiophen-5-yl)methoxy]benzene-methanamine hydrochloride) and other sterol biosynthesis inhibitors such as DMP-565. Preferred HMG CoA reductase inhibitors include lovastatin, pravastatin and **simvastatin**. The most preferred HMG CoA reductase inhibitor is **simvastatin**.
DETD . . . subjects and can be useful in the treatment and/or prevention of vascular conditions, such as vascular inflammation, atherosclerosis, hypercholesterolemia and **sitosterolemia**, stroke, obesity and lowering of plasma levels of cholesterol in subjects, in particular in humans.

L10 ANSWER 6 OF 19 USPATFULL on STN
AB Hypocholesterolemic substituted 2-azetidinone compounds of the formula: ##STR1##

are disclosed, as well as a methods of lowering cholesterol by administering said compounds, pharmaceutical compositions containing them, and the combination of a substituted 2-azetidinone cholesterol-lowering agent and a cholesterol biosynthesis inhibitor for the treatment and prevention of atherosclerosis.
AN 2003:153360 USPATFULL
TI Substituted 2-azetidinones useful as hypocholesterolemic agents
IN Ghosal, Anima, Edison, NJ, UNITED STATES
Zbaida, Shmuel, East Brunswick, NJ, UNITED STATES
Chowdhury, Swapan K., Warren, NJ, UNITED STATES
Iannucci, Robert M., Hampton, NJ, UNITED STATES
Feng, Wenqing, Chatham, NJ, UNITED STATES
Alton, Kevin B., Cedar Knolls, NJ, UNITED STATES
Patrick, James E., Belle Mead, NJ, UNITED STATES
Davis, Harry R., Berkeley Heights, NJ, UNITED STATES
PA Schering Corporation (U.S. corporation)
PI US 2003105028 A1 20030605
AI US 2002-166942 A1 20020611 (10)
RLI Continuation-in-part of Ser. No. US 2001-23295, filed on 17 Dec 2001, PENDING
PRAI US 2000-256875P 20001220 (60)
DT Utility
FS APPLICATION
LREP SCHERING-PLOUGH CORPORATION, PATENT DEPARTMENT (K-6-1, 1990), 2000 GALLOPING HILL ROAD, KENILWORTH, NJ, 07033-0530
CLMN Number of Claims: 36

ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 1603
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

SUMM . . . halting of progression of one or more conditions, for example vascular conditions, such as hyperlipidaemia (for example atherosclerosis, hypercholesterolemia or **sitosterolemia**), vascular inflammation, stroke, diabetes, obesity and/or to reduce the level of sterol(s) (such as cholesterol) in the plasma. As used. . .

SUMM . . . MEVACOR.RTM. which is available from Merck & Co.), pravastatin (for example PRAVACHOL.RTM. which is available from Bristol Meyers Squibb), fluvastatin, **simvastatin** (for example ZOCOR.RTM. which is available from Merck & Co.), atorvastatin, cerivastatin, CI-981, ZD4522, rivastatin (sodium 7-(4-fluorophenyl)-2,6-diisopropyl-5-methoxymethylpyridin-3-yl)-3,5-dihydroxy-6-heptanoate), rosuvastatin, pitavastatin (such. . . hydrochloride) and other sterol biosynthesis inhibitors such as DMP-565. Preferred HMG CoA reductase inhibitors include lovastatin, pravastatin, fluvastatin, atorvastatin and **simvastatin**. The most preferred HMG CoA reductase inhibitor is **simvastatin**.

SUMM . . . and can be useful in the treatment and/or prevention of conditions, for example vascular conditions, such as atherosclerosis, hypercholesterolemia and **sitosterolemia**, stroke, obesity and lowering of plasma levels of cholesterol in mammals, in particular in humans.

CLM What is claimed is:

. . . composition according to claim 21, wherein the cholesterol biosynthesis inhibitor is selected from the group consisting of lovastatin, pravastatin, fluvastatin, **simvastatin**, atorvastatin, L-659,699, squalestatin 1, NB-598, pitavastatin and ZD4522.

23. The pharmaceutical composition according to claim 22, wherein the cholesterol biosynthesis inhibitor is **simvastatin**.

26. The method according to claim 25, wherein the cholesterol biosynthesis inhibitor is selected from the group consisting of lovastatin, pravastatin, fluvastatin, **simvastatin**, atorvastatin, L-659,699, squalestatin 1, NB-598, pitavastatin and ZD4522.

27. The method according to claim 26, wherein the cholesterol biosynthesis inhibitor is **simvastatin**.

31. The pharmaceutical composition according to claim 30, wherein the cholesterol biosynthesis inhibitor is selected from the group consisting of lovastatin, pravastatin, fluvastatin, **simvastatin**, atorvastatin, L-659,699, squalestatin 1, NB-598, pitavastatin and ZD4522.

32. The pharmaceutical composition according to claim 31, wherein the cholesterol biosynthesis inhibitor is **simvastatin**.

35. The method according to claim 34, wherein the cholesterol biosynthesis inhibitor is selected from the group consisting of lovastatin, pravastatin, fluvastatin, **simvastatin**, atorvastatin, L-659,699, squalestatin 1, NB-598, pitavastatin and ZD4522.

36. The method according to claim 35, wherein the cholesterol biosynthesis inhibitor is **simvastatin**.

IT 29066-42-0, L 659699 75330-75-5, Lovastatin **79902-63-9**, Simvastatin 81093-37-0, Pravastatin 93957-54-1, Fluvastatin

131060-14-5, NB-598 134523-00-5, Atorvastatin 142561-96-4, Squalestatin 1 147098-20-2, ZD4522 147511-69-1, Pitavastatin (prepn. of azetidinone glucuronide derivs. and their use as hypocholesterolemic agents combined with a cholesterol biosynthesis inhibitor for treating diabetes, obesity, vascular conditions, and lowering plasma sterol concns.)

L10 ANSWER 7 OF 19 USPATFULL on STN

AB The present invention provides compositions, therapeutic combinations and methods including: (a) at least one sterol absorption inhibitor and (b) at least one cardiovascular agent different from the sterol absorption inhibitor, which can be useful for treating vascular conditions, obesity, diabetes and lowering plasma levels of sterols.

AN 2003:100110 USPATFULL

TI Combinations of sterol absorption inhibitor(s) with cardiovascular agent(s) for the treatment of vascular conditions

IN Kosoglou, Teddy, Jamison, PA, UNITED STATES
Ress, Rudyard J., Flemington, NJ, UNITED STATES
Strony, John T., Lebanon, NJ, UNITED STATES
Veltri, Enrico P., Princeton, NJ, UNITED STATES
Hauer, William, Warren, NJ, UNITED STATES

PA Schering Corporation (U.S. corporation)

PI US 2003069221 A1 20030410

AI US 2002-57339 A1 20020125 (10)

PRAI US 2001-323842P 20010921 (60)
US 2001-264396P 20010126 (60)
US 2001-264600P 20010126 (60)
US 2001-264275P 20010126 (60)

DT Utility

FS APPLICATION

LREP SCHERING-PLOUGH CORPORATION, PATENT DEPARTMENT (K-6-1, 1990), 2000 GALLOPING HILL ROAD, KENILWORTH, NJ, 07033-0530

CLMN Number of Claims: 49

ECL Exemplary Claim: 1

DRWN No Drawings

LN.CNT 3423

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

SUMM . . . in a therapeutically effective amount to treat vascular conditions such as atherosclerosis, hyperlipidaemia (including but not limited to hypercholesterolaemia, hypertriglyceridaemia, **sitosterolemia**), hypertension, vascular inflammation, angina, cardiac arrhythmias, stroke, as well as diabetes, obesity, and/or to reduce the level of sterol(s) in. . .

SUMM . . . agent(s) and sterol absorption inhibitor(s), to prevent or treat a vascular condition, such as hyperlipidaemia (for example atherosclerosis, hypercholesterolemia or **sitosterolemia**), stroke, diabetes, obesity and/or reduce the level of sterol(s) in the plasma. As used herein, "vascular" comprises cardiovascular, cerebrovascular and. . .

SUMM . . . MEVACOR.RTM. which is available from Merck & Co.), pravastatin (for example PRAVACHOL.RTM. which is available from Bristol Meyers Squibb), fluvastatin, **simvastatin** (for example ZOCOR.RTM. which is available from Merck & Co.), atorvastatin, cerivastatin, rosuvastatin, rivastatin (sodium 7-(4-fluorophenyl)-2,6-diisopropyl-5-methoxymethylpyridin-3-yl)-3,5-dihydroxy-6-heptanoate, CI-981 and pitavastatin (such. . . NB-598 ((E)--N-ethyl-N-(6,6-dimethyl-2-hepten-4-ynyl)-3-[(3,3'-bithiophen-5-yl)methoxy]benzene-methanamine hydrochloride) and other sterol biosynthesis inhibitors such as DMP-565. Preferred HMG CoA reductase inhibitors include lovastatin, pravastatin and **simvastatin**. The most preferred HMG CoA reductase inhibitor is **simvastatin**.

SUMM . . . Preferably the cholesterol biosynthesis inhibitor comprises one or more HMG CoA reductase inhibitors, such as, for example, lovastatin, pravastatin and/or **simvastatin**.

DETD . . . below, and can be useful in the treatment and/or prevention of vascular conditions, such as vascular inflammation, atherosclerosis, hypercholesterolemia and **sitosterolemia**, stroke, obesity and lowering of plasma levels of cholesterol in mammals, in particular in humans.

CLM What is claimed is:

. . . 37. The composition according to claim 36 wherein the at least one HMG CoA reductase inhibitor comprises lovastatin, pravastatin, fluvastatin, **simvastatin**, atorvastatin, rosuvastatin, rivastatin, cerivastatin and mixtures thereof.

38. The composition according to claim 37, wherein the at least one HMG CoA reductase inhibitor comprises **simvastatin**.

IT 59-67-6, Nicotinic acid, biological studies 637-07-0, Clofibrate 943-45-3D, Fibric acid, derivs. 5868-05-3, Niceritrol 11041-12-6, Cholestyramine 15351-13-0, Nicofuranose 23288-49-5, Probucol 25812-30-0, Gemfibrozil 30299-08-2, Clinofibrate 41859-67-0, Bezafibrate 49562-28-9, Fenofibrate 50925-79-6, Colestipol 51037-30-0, Acipimox 52214-84-3, Ciprofibrate 69047-39-8, Binifibrate 75330-75-5, Lovastatin **79902-63-9**, Simvastatin 81093-37-0, Pravastatin 93957-54-1, Fluvastatin 96609-16-4, Lifibrol 134523-00-5, Atorvastatin 145599-86-6, Cerivastatin
(combinations of nicotinic acid and derivs. and azetidine sterol absorption inhibitor(s) for treatment of vascular indications)

L10 ANSWER 8 OF 19 USPATFULL on STN

AB The present invention provides compositions, therapeutic combinations and methods including: (a) at least one bile acid sequestrant; and (b) at least one substituted azetidinone or substituted .beta.-lactam sterol absorption inhibitor which can be useful for treating vascular conditions, diabetes, obesity and lowering plasma levels of sterols.

AN 2003:78061 USPATFULL

TI Combinations of bile acid sequestrant(s) and sterol absorption inhibitor(s) and treatments for vascular indications

IN Davis, Harry R., Berkeley Heights, NJ, UNITED STATES
Kosoglou, Teddy, Jamison, PA, UNITED STATES

PA Schering Corporation (U.S. corporation)

PI US 2003053981 A1 20030320

AI US 2002-57534 A1 20020125 (10)

PRAI US 2001-264600P 20010126 (60)
US 2001-323842P 20010921 (60)

DT Utility

FS APPLICATION

LREP SCHERING-PLOUGH CORPORATION, PATENT DEPARTMENT (K-6-1, 1990), 2000 GALLOPING HILL ROAD, KENILWORTH, NJ, 07033-0530

CLMN Number of Claims: 81

ECL Exemplary Claim: 1

DRWN No Drawings

LN.CNT 4194

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

SUMM . . . halting of progression of one or more conditions, for example vascular conditions, such as hyperlipidemia (for example atherosclerosis, hypercholesterolemia or **sitosterolemia**), vascular inflammation, stroke, diabetes, obesity and/or to reduce the level of sterol(s) (such as cholesterol) in the plasma.

SUMM . . . inhibitor(s), to prevent or treat a condition, for example a vascular condition, such as hyperlipidaemia (for example atherosclerosis, hypercholesterolemia or **sitosterolemia**), stroke, diabetes, obesity and/or reduce the level of sterol(s) in the plasma. As used herein, "vascular" comprises cardiovascular, cerebrovascular and. . .

SUMM . . . MEVACOR.RTM. which is available from Merck & Co.), pravastatin (for example PRAVACHOL.RTM. which is available from Bristol Meyers

Squibb), fluvastatin, **simvastatin** (for example ZOCOR.RTM. which is available from Merck & Co.), atorvastatin, cerivastatin, CI-981 and pitavastatin (such as NK-104 of Negma. . . NB-598 ((E)-N-ethyl-N-(6,6-dimethyl-2-hepten-4-ynyl)-3-[(3,3'-bithiophen-5-yl)methoxy]benzene-methanamine hydrochloride) and other sterol biosynthesis inhibitors such as DMP-565. Preferred HMG CoA reductase inhibitors include lovastatin, pravastatin and **simvastatin**. The most preferred HMG CoA reductase inhibitor is **simvastatin**.

SUMM . . . Preferably the cholesterol biosynthesis inhibitor comprises one or more HMG CoA reductase inhibitors, such as, for example, lovastatin, pravastatin and/or **simvastatin**. More preferably, the composition or treatment comprises the compound of Formula (II) in combination with **simvastatin** and cholestyramine or colestipol.

SUMM . . . in a therapeutically effective amount to treat vascular conditions such as atherosclerosis, hyperlipidaemia (including but not limited to hypercholesterolaemia, hypertriglyceridaemia, **sitosterolemia**), stroke, diabetes, obesity, and/or reduce the level of sterol(s) in the plasma. The compositions and treatments can be administered by. . .

DETD . . . cholesterol in mammals, and can be useful in the treatment and/or prevention of vascular conditions, such as atherosclerosis, hypercholesterolemia and **sitosterolemia**, stroke, diabetes, obesity and lowering of plasma levels of cholesterol in mammals, in particular in mammals.

CLM What is claimed is:

. . . 9, wherein the at least one HMG CoA reductase inhibitor is selected from the group consisting of lovastatin, pravastatin, fluvastatin, **simvastatin**, atorvastatin, cerivastatin and mixtures thereof.

11. The composition according to claim 10, wherein the at least one HMG CoA reductase inhibitor is **simvastatin**.

IT 59-67-6, Nicotinic acid, biological studies 637-07-0, Clofibrate 943-45-3D, Fibric acid, derivs. 5868-05-3, Niceritrol 11041-12-6, Cholestyramine 15351-13-0, Nicofuranose 23288-49-5, Probucol 25812-30-0, Gemfibrozil 30299-08-2, Clinofibrate 41859-67-0, Bezafibrate 49562-28-9, Fenofibrate 50925-79-6, Colestipol 51037-30-0, Acipimox 52214-84-3, Ciprofibrate 69047-39-8, Binifibrate 75330-75-5, Lovastatin **79902-63-9**, Simvastatin 81093-37-0, Pravastatin 93957-54-1, Fluvastatin 96609-16-4, Lifibrol 134523-00-5, Atorvastatin 145599-86-6, Cerivastatin
(combinations of nicotinic acid and derivs. and azetidine sterol absorption inhibitor(s) for treatment of vascular indications)

L10 ANSWER 9 OF 19 EMBASE COPYRIGHT 2003 ELSEVIER INC. ALL RIGHTS RESERVED. on STN

AB OBJECTIVE: To review the primary literature describing the pharmacology of ezetimibe and clinical trials investigating its use in the management of hypercholesterolemia. DATA SOURCES: A MEDLINE search (1966-December 2002) was performed using SCH 48461, SCH 58235, ezetimibe, and 2-azetidinone as key words. English-language articles were identified and the references of these articles were used to further identify pertinent articles and abstracts. Given the paucity of published articles available on ezetimibe, many of the references cited are abstracts. STUDY SELECTION: All acquired articles that discussed the pharmacology, pharmacokinetics, chemistry, and clinical efficacy of ezetimibe were reviewed. DATA EXTRACTION: Articles were selected based on content regarding the medicinal chemistry, pharmacology, and clinical use of ezetimibe. DATA SYNTHESIS: Ezetimibe, approved for use in October 2002, belongs to a new class of antihyperlipidemic agents that uniquely inhibit the absorption of cholesterol by inhibiting the cholesterol transport system located within intestinal cell walls. In humans, ezetimibe reduced cholesterol absorption by >50%. In clinical trials, ezetimibe 10 mg/d reduced low-density lipoprotein cholesterol (LDL-C) by approximately 18% and further enhanced

the LDL-C-lowering effect of statin medications by an additional 15-20%. In addition, ezetimibe lowered triglycerides about 5% and increased high-density lipoprotein cholesterol (HDL-C) approximately 3%. Ezetimibe is well tolerated. At present, no serious adverse effects have been directly attributable to ezetimibe. CONCLUSIONS: Based on the data currently available, it appears that ezetimibe has a potential role in the treatment of primary hypercholesterolemia; however further data are needed to determine its long-term tolerability and efficacy. The potential roles for ezetimibe include its concurrent use with a statin to further enhance the lowering of LDL-C. Other possible roles for ezetimibe include its concurrent use with a statin to permit a lowering of statin dosage to avoid statin-related complications or its use as monotherapy to treat hypercholesterolemia when statin use cannot be tolerated or is contraindicated. Outcome data demonstrating that cardiovascular morbidity and/or mortality are reduced by ezetimibe therapy have yet to be generated.

AN 2003213660 EMBASE

TI Ezetimibe for management of hypercholesterolemia.

AU Mauro V.F.; Tuckerman C.E.

CS C.E. Tuckerman, Pharmacy Services, Medical College of Ohio, 3000 Arlington Ave., Toledo, OH 43614-2589, United States. ctuckerman@mco.edu

SO Annals of Pharmacotherapy, (1 Jun 2003) 37/6 (839-848).
Refs: 64
ISSN: 1060-0280 CODEN: APHRER

CY United States

DT Journal; General Review

FS 018 Cardiovascular Diseases and Cardiovascular Surgery
037 Drug Literature Index
038 Adverse Reactions Titles

LA English

SL English; Spanish; French

CT Medical Descriptors:
*hypercholesterolemia: DT, drug therapy
sitosterolemia: DT, drug therapy
metabolic disorder: DT, drug therapy
MEDLINE
cholesterol metabolism
cholesterol blood level
drug tolerability
cardiovascular disease
drug structure
drug half life
dose response
wrist disease: SI, side effect
thorax. . .
A reductase inhibitor
triacylglycerol: EC, endogenous compound
high density lipoprotein cholesterol: EC, endogenous compound
mevinolin: CB, drug combination
mevinolin: CM, drug comparison
mevinolin: DT, drug therapy
placebo
simvastatin: CB, drug combination
simvastatin: CM, drug comparison
simvastatin: DO, drug dose
simvastatin: DT, drug therapy
fenofibrate: CM, drug comparison
fenofibrate: IT, drug interaction
fenofibrate: DT, drug therapy
atorvastatin: CB, drug combination
atorvastatin: CM, drug comparison
atorvastatin: DO, drug. . .

RN (ezetimibe) 163222-33-1; (1,4 bis(4 methoxyphenyl) 3 (3 phenylpropyl) 2 azetidinone) 148260-92-8; (statine) 49642-07-1; (mevinolin) 75330-75-5; (

simvastatin) 79902-63-9; (fenofibrate) 49562-28-9; (atorvastatin) 134523-00-5, 134523-03-8; (fluindostatin) 93957-54-1; (pravastatin) 81131-74-0; (sitosterol) 19044-06-5, 83-46-5; (campesterol) 474-62-4; (caffeine) 30388-07-9, 58-08-2; (tolbutamide) 473-41-6,. . .

L10 ANSWER 10 OF 19 CAPLUS COPYRIGHT 2003 ACS on STN DUPLICATE 1

AB Background/Aim: Mutations in genes encoding the ATP-binding cassette (ABC)-transporters ABCG5 and ABCG8 underlie **sitosterolemia**, which is characterized by elevated plasma levels of phytosterols due to increased intestinal absorption and impaired biliary secretion of sterols. The aim of our study was to correlate the expression levels of Abcg5 and Abcg8 to biliary cholesterol secretion in various (genetically-modified) mouse models. Methods: Bile was collected from genetically-modified mice fed a chow diet, or from mice fed either a chow diet, or chow supplemented with either 1% diosgenin, 0.1% **simvastatin**, or a synthetic liver X receptor agonist, for detn. of biliary lipids. Livers and small intestines were harvested and expression levels of Abcg5, Abcg8 and Abcb4 were detd. by real-time polymerase chain reaction. Results: Intestinal expression of Abcg5 and Abcg8 did not show much variation between the various models. In contrast, a linear correlation between hepatic expression levels of Abcg5 and Abcg8 and biliary cholesterol secretion rates was found. This relation was independent of Abcb4-mediated phospholipid secretion. However, in diosgenin-fed mice showing cholesterol hypersecretion, hepatic Abcg5 and Abcg8 expression levels remained unchanged. Conclusions: Our results strongly support a role for Abcg5 and Abcg8 in regulation of biliary cholesterol secretion, but also indicate the existence of a largely independent route of cholesterol secretion.

AN 2003:391414 CAPLUS

TI Relation between hepatic expression of ATP-binding cassette transporters G5 and G8 and biliary cholesterol secretion in mice

AU Kosters, Astrid; Frijters, Raoul J. J. M.; Schaap, Frank G.; Vink, Edwin; Plosch, Torsten; Ottenhoff, Roelof; Jirsa, Milan; De Cuyper, Iris M.; Kuipers, Folkert; Groen, Albert K.

CS AMC Liver Center, Department of Experimental Hepatology, Academic Medical Center, Amsterdam, 1105 BK, Neth.

SO Journal of Hepatology (2003), 38(6), 710-716
CODEN: JOHEEC; ISSN: 0168-8278

PB Elsevier Science Ltd.

DT Journal

LA English

RE.CNT 34 THERE ARE 34 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

AB Background/Aim: Mutations in genes encoding the ATP-binding cassette (ABC)-transporters ABCG5 and ABCG8 underlie **sitosterolemia**, which is characterized by elevated plasma levels of phytosterols due to increased intestinal absorption and impaired biliary secretion of sterols. The aim of our study was to correlate the expression levels of Abcg5 and Abcg8 to biliary cholesterol secretion in various (genetically-modified) mouse models. Methods: Bile was collected from genetically-modified mice fed a chow diet, or from mice fed either a chow diet, or chow supplemented with either 1% diosgenin, 0.1% **simvastatin**, or a synthetic liver X receptor agonist, for detn. of biliary lipids. Livers and small intestines were harvested and expression levels of Abcg5, Abcg8 and Abcb4 were detd. by real-time polymerase chain reaction. Results: Intestinal expression of Abcg5 and Abcg8 did not show much variation between the various models. In contrast, a linear correlation between hepatic expression levels of Abcg5 and Abcg8 and biliary cholesterol secretion rates was found. This relation was independent of Abcb4-mediated phospholipid secretion. However, in diosgenin-fed mice showing cholesterol hypersecretion, hepatic Abcg5 and Abcg8 expression levels remained unchanged. Conclusions: Our results strongly support a role for Abcg5 and Abcg8 in regulation of biliary cholesterol secretion, but also indicate the existence of a largely independent route of cholesterol

secretion.

L10 ANSWER 11 OF 19 CAPLUS COPYRIGHT 2003 ACS on STN DUPLICATE 2
AB A review. Ezetimibe, a synthetic 2-azetidinone, is the first of a new class of compds. that selectively inhibits the absorption of cholesterol and related plant sterols in the intestine. The drug, and its glucuronyl metabolite, are thought to inhibit a putative cholesterol transporter of enterocytes, located within the brush-border membrane of the small intestine. In large, randomized, placebo-controlled, 12-wk trials, ezetimibe reduced levels of low d. lipoprotein-cholesterol (LDL-C) by approx. 18%; triglyceride levels were reduced by approx. 6% in one trial but not another. Ezetimibe produced a modest increase in levels of high d. lipoprotein-cholesterol. Moreover, redns. in LDL-C and triglyceride levels were greater in patients treated with ezetimibe coadministered with a statin (lovastatin, pravastatin, atorvastatin or **simvastatin**), than with either of those agents given alone. The coadministration of the lowest statin dose and ezetimibe produced similar LDL-C redns. to the administration of the highest statin dose alone. Ezetimibe also provided beneficial effects on plasma lipid levels when administered to patients with hypercholesterolemia already receiving a statin. Ezetimibe plus a statin reduced LDL-C levels more than the max. statin dose alone in a trial in patients with homozygous familial hypercholesterolemia and was effective in a placebo-controlled trial in patients with homozygous **sitosterolemia**. The drug was well tolerated in clin. studies conducted to date. In large, randomized, double-blind trials, ezetimibe had a similar tolerability profile to that of placebo. Coadministration of ezetimibe and a statin did not increase the incidence of adverse events related to statin monotherapy.
AN 2003:177555 CAPLUS
DN 138:362015
TI Ezetimibe
AU Darkes, Malcolm J. M.; Poole, Raewyn M.; Goa, Karen L.
CS Adis International Inc., Langhorne, PA, USA
SO American Journal of Cardiovascular Drugs (2003), 3(1), 67-76
CODEN: AJCDDJ; ISSN: 1175-3277
PB Adis International Ltd.
DT Journal; General Review
LA English
RE.CNT 68 THERE ARE 68 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT
AB A review. Ezetimibe, a synthetic 2-azetidinone, is the first of a new class of compds. that selectively inhibits the absorption of cholesterol and related plant sterols in the intestine. The drug, and its glucuronyl metabolite, are thought to inhibit a putative cholesterol transporter of enterocytes, located within the brush-border membrane of the small intestine. In large, randomized, placebo-controlled, 12-wk trials, ezetimibe reduced levels of low d. lipoprotein-cholesterol (LDL-C) by approx. 18%; triglyceride levels were reduced by approx. 6% in one trial but not another. Ezetimibe produced a modest increase in levels of high d. lipoprotein-cholesterol. Moreover, redns. in LDL-C and triglyceride levels were greater in patients treated with ezetimibe coadministered with a statin (lovastatin, pravastatin, atorvastatin or **simvastatin**), than with either of those agents given alone. The coadministration of the lowest statin dose and ezetimibe produced similar LDL-C redns. to the administration of the highest statin dose alone. Ezetimibe also provided beneficial effects on plasma lipid levels when administered to patients with hypercholesterolemia already receiving a statin. Ezetimibe plus a statin reduced LDL-C levels more than the max. statin dose alone in a trial in patients with homozygous familial hypercholesterolemia and was effective in a placebo-controlled trial in patients with homozygous **sitosterolemia**. The drug was well tolerated in clin. studies conducted to date. In large, randomized, double-blind trials, ezetimibe had a similar tolerability profile to that of placebo. Coadministration of ezetimibe and a statin did not increase the incidence of adverse events

related to statin monotherapy.

L10 ANSWER 12 OF 19 CAPLUS COPYRIGHT 2003 ACS on STN
AB The invention discloses the use of sterol absorption-inhibiting compds., pharmaceutical compns. thereof, therapeutic combinations, and their use in combination with other lipid-lowering agents to treat or prevent **sitosterolemia** and/or to lower the concn. of sterol(s) other than cholesterol in plasma or tissue of a mammal. Methods of treating or preventing vascular disease and coronary events also are provided. The methodol. and compns. of the invention use substituted azetidinone compds., e.g. I (prepn. described).
AN 2002:574926 CAPLUS
DN 137:135094
TI The use of substituted azetidinone compounds for the treatment of **sitosterolemia**
IN Davis, Harry R.
PA Schering Corporation, USA
SO PCT Int. Appl., 105 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2002058696	A2	20020801	WO 2002-US1195	20020125
	WO 2002058696	A3	20030313		
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, HR, HU, ID, IL, IN, IS, JP, KG, KR, KZ, LC, LK, LR, LT, LU, LV, MA, MD, MG, MK, MN, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UZ, VN, YU, ZA, ZM, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	US 2002169134	A1	20021114	US 2002-57629	20020125
PRAI	US 2001-264645P	P	20010126		

OS MARPAT 137:135094
TI The use of substituted azetidinone compounds for the treatment of **sitosterolemia**
AB The invention discloses the use of sterol absorption-inhibiting compds., pharmaceutical compns. thereof, therapeutic combinations, and their use in combination with other lipid-lowering agents to treat or prevent **sitosterolemia** and/or to lower the concn. of sterol(s) other than cholesterol in plasma or tissue of a mammal. Methods of treating or preventing vascular disease and coronary events also are provided. The methodol. and compns. of the invention use substituted azetidinone compds., e.g. I (prepn. described).
ST azetidinone deriv prepn **sitosterolemia** treatment; noncholesterol sterol redn azetidinone deriv; vascular disease coronary event treatment azetidinone deriv
IT Apolipoproteins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(E, apoE knockout mouse; azetidinone derivs. for treatment of **sitosterolemia**)
IT Antiarteriosclerotics
(antiatherosclerotics; azetidinone derivs. for treatment of **sitosterolemia**)
IT Antiarteriosclerotics
Arteriosclerosis
Atherosclerosis
Blood vessel, disease
Cardiovascular agents
Cardiovascular system, disease

Drug delivery systems
Human
Hypolipemic agents
(azetidinone derivs. for treatment of **sitosterolemia**)

IT Sterols
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(azetidinone derivs. for treatment of **sitosterolemia**)

IT Sequestering agents
(bile acid; azetidinone derivs. for treatment of **sitosterolemia**
)

IT Drug delivery systems
(capsules; azetidinone derivs. for treatment of **sitosterolemia**
)

IT Artery, disease
(coronary; azetidinone derivs. for treatment of **sitosterolemia**
)

IT Liver
(hepatic sitosterol accumulation; azetidinone derivs. for treatment of **sitosterolemia**)

IT Lipoproteins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(low-d.; azetidinone derivs. for treatment of **sitosterolemia**)

IT Lipids, biological studies
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(metabolic disorders; azetidinone derivs. for treatment of **sitosterolemia**)

IT Embryophyta
(phytosterols; azetidinone derivs. for treatment of **sitosterolemia**)

IT Natural products
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(phytosterols; azetidinone derivs. for treatment of **sitosterolemia**)

IT Drug delivery systems
(prodrugs; azetidinone derivs. for treatment of **sitosterolemia**
)

IT Bile acids
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(sequestrants; azetidinone derivs. for treatment of **sitosterolemia**)

IT Sterols
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(stanols, 5.alpha.-; azetidinone derivs. for treatment of **sitosterolemia**)

IT Drug delivery systems
(tablets; azetidinone derivs. for treatment of **sitosterolemia**
)

IT Biological transport
(uptake; azetidinone derivs. for treatment of **sitosterolemia**)

IT 57-88-5, Cholesterol, biological studies
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(LDL; azetidinone derivs. for treatment of **sitosterolemia**)

IT 80-97-7, Cholestanol 83-45-4, Sitostanol 83-46-5 83-48-7, Stigmasterol 474-60-2, Campestanol 474-62-4, Campesterol 23290-26-8, Avenasterol
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(azetidinone derivs. for treatment of **sitosterolemia**)

IT 163222-33-1P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(azetidinone derivs. for treatment of **sitosterolemia**)

IT 11041-12-6, Cholestyramine 50925-79-6, Colestipol 75330-75-5, Lovastatin **79902-63-9**, **Simvastatin** 81093-37-0,

Pravastatin 93957-54-1, Fluvastatin 134523-00-5, Atorvastatin 147511-69-1, Itavastatin 163222-33-1D, prodrug derivs. 182815-44-7, Colesevelam hydrochloride 287714-41-4, Rosuvastatin 438576-91-1 438576-91-1D, derivs. 438576-92-2 438576-92-2D, prodrug derivs. 444313-49-9 444313-50-2 444313-51-3 444313-53-5 444313-55-7 444313-57-9 444313-59-1 444313-60-4 444313-61-5 444313-62-6
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(azetidinone derivs. for treatment of **sitosterolemia**)

IT 9028-35-7, HMG-CoA reductase
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(inhibitors; azetidinone derivs. for treatment of **sitosterolemia**)

IT 163222-32-0P 163380-15-2P 191330-56-0P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. and reaction; azetidinone derivs. for treatment of **sitosterolemia**)

IT 112022-81-8 112022-83-0 133472-27-2, 4-Fluorophenylzinc chloride
RL: RCT (Reactant); RACT (Reactant or reagent)
(reaction; azetidinone derivs. for treatment of **sitosterolemia**)

L10 ANSWER 13 OF 19 USPATFULL on STN

AB The present invention provides compositions, therapeutic combinations and methods including: (a) at least one peroxisome proliferator-activated receptor activator; and (b) at least one substituted azetidinone or substituted .beta.-lactam sterol absorption inhibitor which can be useful for treating vascular conditions, diabetes, obesity and lowering plasma levels of sterols.

AN 2002:336849 USPATFULL

TI Sterol absorption inhibitor compositions

IN Cho, Wing-Kee Philip, Princeton, NJ, UNITED STATES
Davis, Harry R., Berkeley Heights, NJ, UNITED STATES
Kosoglou, Teddy, Jamison, PA, UNITED STATES
Picard, Gilles J., Braine L'Alleud, BELGIUM

PI US 2002192203 A1 20021219

AI US 2002-136968 A1 20020501 (10)

RLI Division of Ser. No. US 2002-57323, filed on 25 Jan 2002, PENDING

PRAI US 2001-264396P 20010126 (60)
US 2001-323839P 20010921 (60)

DT Utility

FS APPLICATION

LREP SCHERING-PLOUGH CORPORATION, PATENT DEPARTMENT (K-6-1, 1990), 2000 GALLOPING HILL ROAD, KENILWORTH, NJ, 07033-0530

CLMN Number of Claims: 101

ECL Exemplary Claim: 1

DRWN No Drawings

LN.CNT 4987

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

SUMM . . . halting of progression of one or more conditions, for example vascular conditions, such as hyperlipidaemia (for example atherosclerosis, hypercholesterolemia or **sitosterolemia**), vascular inflammation, stroke, diabetes, obesity and/or to reduce the level of sterol(s) (such as cholesterol) in the plasma.

SUMM . . . inhibitor(s), to prevent or treat a condition, for example a vascular condition, such as hyperlipidaemia (for example atherosclerosis, hypercholesterolemia or **sitosterolemia**), vascular inflammation, stroke, diabetes, obesity and/or reduce the level of sterol(s) (such as cholesterol) in the plasma. As used herein,. . .

SUMM . . . MEVACOR.RTM. which is available from Merck & Co.), pravastatin (for example PRAVACHOL.RTM. which is available from Bristol Meyers Squibb), fluvastatin, **simvastatin** (for example ZOCOR.RTM. which is available from Merck & Co.), atorvastatin, cerivastatin,

CI-981, rivastatin (sodium 7-(4-fluorophenyl)-2,6-diisopropyl-5-methoxymethylpyridin-3-yl)-3,5-dihydroxy-6-heptanoate), rosuvastatin, pitavastatin (such as. . . NB-598 ((E)--N-ethyl-N-(6,6-dimethyl-2-hepten-4-ynyl)-3-[(3,3'-bithiophen-5-yl)methoxy]benzene-methanamine hydrochloride) and other sterol biosynthesis inhibitors such as DMP-565. Preferred HMG CoA reductase inhibitors include lovastatin, pravastatin and **simvastatin**. The most preferred HMG CoA reductase inhibitor is **simvastatin**.

SUMM . . . Preferably the cholesterol biosynthesis inhibitor comprises one or more HMG CoA reductase inhibitors, such as, for example, lovastatin, pravastatin and/or **simvastatin**. More preferably, the composition or treatment comprises the compound of Formula (II) in combination with **simvastatin** and gemfibrozil or fenofibrate.

SUMM . . . treat one or more conditions, for example vascular conditions such as atherosclerosis, hyperlipidaemia (including but not limited to hypercholesterolemia, hypertriglyceridaemia, **sitosterolemia**), vascular inflammation, stroke, diabetes, obesity, and/or reduce the level of sterol(s) in the plasma. The compositions and treatments can be. . .

DETD . . . and can be useful in the treatment and/or prevention of conditions, for example vascular conditions, such as atherosclerosis, hypercholesterolemia and **sitosterolemia**, stroke, obesity and lowering of plasma levels of cholesterol in mammals, in particular in mammals.

CLM What is claimed is:

. . . 15, wherein the at least one HMG CoA reductase inhibitor is selected from the group consisting of lovastatin, pravastatin, fluvastatin, **simvastatin**, atorvastatin, rosuvastatin, cerivastatin and mixtures thereof.

17. The composition according to claim 16, wherein the at least one HMG CoA reductase inhibitor is **simvastatin**.

18. The composition according to claim 12, further comprising **simvastatin**.

46. The composition according to claim 45, wherein the at least one HMG CoA reductase inhibitor is **simvastatin**.

52. The method of claim 51, wherein the HMG CoA reductase inhibitor is **simvastatin**.

IT 59-67-6, Nicotinic acid, biological studies 637-07-0, Clofibrate 943-45-3D, Fibric acid, derivs. 5868-05-3, Niceritrol 11041-12-6, Cholestyramine 15351-13-0, Nicofuranose 23288-49-5, Probucol 25812-30-0, Gemfibrozil 30299-08-2, Clinofibrate 41859-67-0, Bezafibrate 49562-28-9, Fenofibrate 50925-79-6, Colestipol 51037-30-0, Acipimox 52214-84-3, Ciprofibrate 69047-39-8, Binifibrate 75330-75-5, Lovastatin **79902-63-9**, Simvastatin 81093-37-0, Pravastatin 93957-54-1, Fluvastatin 96609-16-4, Lifibrol 134523-00-5, Atorvastatin 145599-86-6, Cerivastatin
(combinations of nicotinic acid and derivs. and azetidine sterol absorption inhibitor(s) for treatment of vascular indications)

L10 ANSWER 14 OF 19 USPATFULL on STN

AB The present invention provides compositions, therapeutic combinations and methods including: (a) at least one of nicotinic acid or derivatives thereof; and (b) at least one substituted azetidinone or substituted .beta.-lactam sterol absorption inhibitor which can be useful for treating vascular conditions, diabetes, obesity and lowering plasma levels of sterols.

AN 2002:323139 USPATFULL

TI Combinations of nicotinic acid and derivatives thereof and sterol absorption inhibitor(s) and treatments for vascular indications

IN Davis, Harry R., Berkeley Heights, NJ, UNITED STATES
Kosoglou, Teddy, Jamison, PA, UNITED STATES
PA Schering Corporation (U.S. corporation)
PI US 2002183305 A1 20021205
AI US 2002-57646 A1 20020125 (10)
PRAI US 2001-264275P 20010126 (60)
US 2001-323842P 20010921 (60)
DT Utility
FS APPLICATION
LREP SCHERING-PLOUGH CORPORATION, PATENT DEPARTMENT (K-6-1, 1990), 2000 GALLOPING HILL ROAD, KENILWORTH, NJ, 07033-0530
CLMN Number of Claims: 81
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 4256
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

SUMM . . . halting of progression of one or more conditions, for example vascular conditions, such as hyperlipidemia (for example atherosclerosis, hypercholesterolemia or **sitosterolemia**), vascular inflammation, stroke, diabetes, obesity and/or to reduce the level of sterol(s) (such as cholesterol) in the plasma.

SUMM . . . inhibitor(s), to prevent or treat a condition, for example a vascular condition, such as hyperlipidaemia (for example atherosclerosis, hypercholesterolemia or **sitosterolemia**), stroke, diabetes, obesity and/or reduce the level of sterol(s) in the plasma. As used herein, "vascular" comprises cardiovascular, cerebrovascular and. . .

SUMM . . . MEVACOR.RTM. which is available from Merck & Co.), pravastatin (for example PRAVACHOL.RTM. which is available from Bristol Meyers Squibb), fluvastatin, **simvastatin** (for example ZOCOR.RTM. which is available from Merck & Co.), atorvastatin, cerivastatin, CI-981, and pitavastatin (such as NK-104 of Negma. . . NB-598 ((E)-N-ethyl-N-(6,6-dimethyl-2-hepten4-ynyl)-3-[(3,3'-bithiophen-5-yl)methoxy]benzene-methanamine hydrochloride) and other sterol biosynthesis inhibitors such as DMP-565. Preferred HMG CoA reductase inhibitors include lovastatin, pravastatin and **simvastatin**. The most preferred HMG CoA reductase inhibitor is **simvastatin**.

SUMM . . . Preferably the cholesterol biosynthesis inhibitor comprises one or more HMG CoA reductase inhibitors, such as, for example, lovastatin, pravastatin and/or **simvastatin**. More preferably, the composition or treatment comprises the compound of Formula (II) in combination with **simvastatin** and nicotinic acid or acipimox.

SUMM . . . in a therapeutically effective amount to treat vascular conditions such as atherosclerosis, hyperlipidaemia (including but not limited to hypercholesterolaemia, hypertriglyceridaemia, **sitosterolemia**), stroke, diabetes, obesity, and/or reduce the level of sterol(s) in the plasma. The compositions and treatments can be administered by. . .

DETD . . . cholesterol in mammals, and can be useful in the treatment and/or prevention of vascular conditions, such as atherosclerosis, hypercholesterolemia and **sitosterolemia**, diabetes, obesity and lowering of plasma levels of cholesterol in mammals, in particular in mammals.

CLM What is claimed is:

. . . 8, wherein the at least one HMG CoA reductase inhibitor is selected from the group consisting of lovastatin, pravastatin, fluvastatin, **simvastatin**, atorvastatin, cerivastatin and mixtures thereof.

10. The composition according to claim 9, wherein the at least one HMG CoA reductase inhibitor is **simvastatin**.

IT 59-67-6, Nicotinic acid, biological studies 637-07-0, Clofibrate 943-45-3D, Fibric acid, derivs. 5868-05-3, Niceritrol 11041-12-6, Cholestyramine 15351-13-0, Nicofuranose 23288-49-5, Probucol

25812-30-0, Gemfibrozil 30299-08-2, Clinofibrate 41859-67-0, Bezafibrate 49562-28-9, Fenofibrate 50925-79-6, Colestipol 51037-30-0, Acipimox 52214-84-3, Ciprofibrate 69047-39-8, Binifibrate 75330-75-5, Lovastatin **79902-63-9**, Simvastatin 81093-37-0, Pravastatin 93957-54-1, Fluvastatin 96609-16-4, Lifibrol 134523-00-5, Atorvastatin 145599-86-6, Cerivastatin
(combinations of nicotinic acid and derivs. and azetidine sterol absorption inhibitor(s) for treatment of vascular indications)

L10 ANSWER 15 OF 19 USPATFULL on STN

AB The present invention is directed to the use of sterol absorption inhibiting compounds, pharmaceutical compositions thereof, therapeutic combinations and their use in combination with other lipid lowering agents to treat or prevent **sitosterolemia** and/or to lower the concentration of sterol(s) other than cholesterol in plasma or tissue of a mammal. Methods of treating or preventing vascular disease and coronary events also are provided.

AN 2002:301589 USPATFULL

TI Use of substituted azetidinone compounds for the treatment of **sitosterolemia**

IN Davis, Harry R., Berkeley Heights, NJ, UNITED STATES

PA Schering Corporation (U.S. corporation)

PI US 2002169134 A1 20021114

AI US 2002-57629 A1 20020125 (10)

PRAI US 2001-264645P 20010126 (60)

DT Utility

FS APPLICATION

LREP SCHERING-PLOUGH CORPORATION, PATENT DEPARTMENT (K-6-1, 1990), 2000 GALLOPING HILL ROAD, KENILWORTH, NJ, 07033-0530

CLMN Number of Claims: 58

ECL Exemplary Claim: 1

DRWN No Drawings

LN.CNT 3321

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

TI Use of substituted azetidinone compounds for the treatment of **sitosterolemia**

AB . . . compounds, pharmaceutical compositions thereof, therapeutic combinations and their use in combination with other lipid lowering agents to treat or prevent **sitosterolemia** and/or to lower the concentration of sterol(s) other than cholesterol in plasma or tissue of a mammal. Methods of treating. . .

SUMM [0002] The present invention provides methods and pharmaceutical compositions for treating or preventing **sitosterolemia** by administering to a mammal in need of such treatment an effective amount of at least one treatment composition comprising. . .

SUMM [0003] **Sitosterolemia** is a genetic lipid storage disorder characterized by increased levels of sitosterol and other plant sterols in the plasma and other tissues due to increased non-selective intestinal absorption of sterols and decreased hepatic removal. Individuals having **sitosterolemia** can exhibit one or more of the following conditions: tendon and tuberous xanthomas, arthritis, hemolytic episodes, accelerated atherosclerosis and myocardial. . . can die at an early age due to extensive coronary atherosclerosis. See Nguyen et al., "Regulation of cholesterol biosynthesis in **sitosterolemia**: effects of lovastatin, cholestyramine, and dietary sterol restriction", Vol 32, Journal of Lipid Research, pp. 1941-1948, (1991), incorporated by reference. . .

SUMM [0004] **Sitosterolemia** can be treated with bile acid sequestrants (such as cholestyramine, colesevelam hydrochloride and colestipol), however, these compounds have a tendency. . .

SUMM [0006] An improved treatment for **sitosterolemia** is needed which can reduce the concentration of sterols in plasma and tissues and inhibit associated debilitating physical effects. Also,. . .

SUMM [0007] The present invention provides a method of treating or preventing

sitosterolemia, comprising administering to a mammal in need of such treatment an effective amount of at least one sterol absorption inhibitor,. . .

SUMM [0008] In another embodiment, the present invention provides a method of treating or preventing **sitosterolemia**, comprising administering to a mammal in need of such treatment: (1) an effective amount of at least one sterol absorption. . .

SUMM [0009] In another embodiment, the present invention provides a method of treating or preventing **sitosterolemia** comprising administering to a mammal in need of such treatment: (1) an effective amount of at least one sterol absorption. . .

SUMM [0010] Other embodiments of the present invention include pharmaceutical compositions for the treatment or prevention of **sitosterolemia** comprising an effective amount of the compositions or combinations used in the methods described above in a pharmaceutically acceptable carrier.

SUMM [0017] The present invention provides methods, pharmaceutical compositions and combinations for treating or preventing **sitosterolemia** and conditions or symptoms associated with **sitosterolemia** such as are discussed above. Another aspect of the present invention provides methods, pharmaceutical compositions and combinations for reducing the. . . be useful in the treatment and/or prevention of vascular conditions or disease, such as vascular inflammation, arteriosclerosis, atherosclerosis, hypercholesterolemia and **sitosterolemia**, and cardiovascular events, stroke and/or obesity.

SUMM . . . for use in the treatment compositions of the present invention include HMG CoA reductase inhibitors such as lovastatin, pravastatin, fluvastatin, **simvastatin**, atorvastatin, rosuvastatin and itavastatin. Preferred HMG CoA reductase inhibitors include lovastatin, atorvastatin and **simvastatin**. The most preferred HMG CoA reductase inhibitors are atorvastatin and **simvastatin**.

SUMM . . . inhibitors. Preferably, the treatment composition comprises one or more HMG CoA reductase inhibitors such as, for example, lovastatin, atorvastatin and **simvastatin** in combination with a compound of Formula (VIII) ##STR56##

SUMM [0357] Still even more preferred, the treatment composition comprises compound of formula VIII in combination with atorvastatin and/or **simvastatin**.

SUMM . . . referred to herein as carrier materials). Because of their sterol absorption inhibitory activity, such pharmaceutical compositions possess utility in treating **sitosterolemia** and related disorders.

SUMM . . . can be administered to a mammal in need of such treatment in a pharmaceutically or therapeutically effective amount to treat **sitosterolemia** and/or reduce the level of sterol(s) in the plasma and tissues.

SUMM . . . therapeutic agents, such as sterol absorption inhibitor(s) and bile acid sequestrant(s) or other therapeutic vascular agents, to prevent or treat **sitosterolemia** and/or reduce the level of sterol(s) in the plasma and tissues. As used herein, "vascular" comprises cardiovascular, cerebrovascular and combinations. . .

SUMM . . . the intestinal absorption of sitosterol and can be useful in the treatment and/or prevention of vascular disease, arteriosclerosis, atherosclerosis and **sitosterolemia** in mammals, in particular in humans.

SUMM [0445] In another embodiment, the present invention provides a method of treating or preventing **sitosterolemia** comprising administering to a mammal in need of such treatment an effective amount of at least one sterol absorption inhibitor. . .

SUMM . . . and the second amount taken together in their totality comprise a therapeutically effective amount for the treatment or prevention of **sitosterolemia** in a mammal.

SUMM . . . be useful in the treatment and/or prevention of vascular conditions or disease, such as vascular inflammation, arteriosclerosis,

atherosclerosis, hypercholesterolemia and **sitosterolemia**, and cardiovascular events, stroke and obesity.

DETD [0475] In a randomized multicenter, double-blind, placebo-controlled, 8-week trial, 37 human patients previously diagnosed with homozygous **sitosterolemia** were randomized to receive Compound VIII (n=30) or placebo (n=7):

DETD . . . T; Kwiterovich, Jr, P O, "Increased sitosterol absorption, decreased removal and expanded body pools compensate for reduced cholesterol synthesis in **sitosterolemia** with xanthomatosis", J Lipid Res, Vol. 30, pp 1319-30, (1989) and Lutjohann, D; Bjorkhem, I; Beil, U F, and von. . .

CLM What is claimed is:

1. A method of treating or preventing **sitosterolemia**, comprising administering to a mammal in need of such treatment an effective amount of at least one sterol absorption inhibitor,. . .

17. The method of claim 16, wherein the HMG-CoA reductase inhibitor is selected from the group consisting of **simvastatin**, lovastatin, pravastatin, fluvastatin, atorvastatin, rosuvastatin, itavastatin and mixtures thereof.

18. The method of claim 17, wherein the HMG-CoA reductase inhibitor is **simvastatin** or atorvastatin.

. . . The method of claim 22, wherein the HMG-CoA reductase inhibitor is selected from the group consisting of lovastatin, pravastatin, fluvastatin, **simvastatin**, atorvastatin, rosuvastatin, itavastatin and mixtures thereof.

24. A method of treating or preventing **sitosterolemia** comprising administering to a mammal in need of such treatment: (a) an effective amount of a sterol absorption inhibitor represented by Formula (VIII): ##STR90## and b) an effective amount of atorvastatin and/or **simvastatin**.

25. A pharmaceutical composition for the treatment or prevention of **sitosterolemia**, comprising an effective amount of the sterol absorption inhibitor used in the method of claim 1 in a pharmaceutically acceptable. . .

26. A pharmaceutical composition for the treatment or prevention of **sitosterolemia**, comprising an effective amount of the sterol absorption inhibitor used in the method of claim 8 in a pharmaceutically acceptable. . .

27. A pharmaceutical composition for the treatment or prevention of **sitosterolemia**, comprising an effective amount of the compound of Formula (VIII) ##STR91## in a pharmaceutically acceptable carrier.

28. A pharmaceutical composition for the treatment or prevention of **sitosterolemia**, comprising: a) an effective amount of the compound of Formula (VIII) ##STR92## and b) an effective amount of a lipid. . .

. . . composition of claim 29, wherein the HMG CoA reductase inhibitor is selected from the group consisting of lovastatin, pravastatin, fluvastatin, **simvastatin**, atorvastatin, rosuvastatin, itavastatin and mixtures thereof.

31. The composition of claim 30, wherein the HMG CoA reductase inhibitor is **simvastatin** or atorvastatin.

32. A method of treating or preventing **sitosterolemia**, comprising administering to a mammal in need of such treatment: (1) an effective amount of at least one sterol absorption. . .

33. A method of treating or preventing **sitosterolemia** comprising administering to a mammal in need of such treatment: (1) an effective amount of at least one sterol absorption. . .

42. The method of claim 41, wherein the HMG CoA reductase inhibitor is **simvastatin** or atorvastatin.

46. A pharmaceutical composition for the treatment or prevention of **sitosterolemia**, comprising: a) an effective amount of the compound of Formula (VIII) ##STR95## and b) an effective amount of a bile. . .

. . . wherein the first amount and the second amount together comprise a therapeutically effective amount for the treatment or prevention of **sitosterolemia** in a mammal.

. . . wherein the first amount and the second amount together comprise a therapeutically effective amount for the treatment or prevention of **sitosterolemia** in a mammal.

IT 11041-12-6, Cholestyramine 50925-79-6, Colestipol 75330-75-5, Lovastatin **79902-63-9**, Simvastatin 81093-37-0, Pravastatin 93957-54-1, Fluvastatin 134523-00-5, Atorvastatin 147511-69-1, Itavastatin 163222-33-1D, prodrug derivs. 182815-44-7, Colesevelam hydrochloride 287714-41-4, Rosuvastatin 438576-91-1 438576-91-1D, derivs. 438576-92-2 438576-92-2D, prodrug derivs. 444313-49-9 444313-50-2 444313-51-3 444313-53-5 444313-55-7 444313-57-9 444313-59-1 444313-60-4 444313-61-5 444313-62-6
(azetidinone derivs. for treatment of sitosterolemia)

L10 ANSWER 16 OF 19 USPATFULL on STN

AB The present invention provides compositions, therapeutic combinations and methods including: (a) at least one peroxisome proliferator-activated receptor activator; and (b) at least one substituted azetidinone or substituted .beta.-lactam sterol absorption inhibitor which can be useful for treating vascular conditions, diabetes, obesity and lowering plasma levels of sterols.

AN 2002:273408 USPATFULL

TI Combinations of peroxisome proliferator-activated receptor (PPAR) activator(s) and sterol absorption inhibitor(s) and treatments for vascular indications

IN Davis, Harry R., Berkeley Heights, NJ, UNITED STATES
Kosoglou, Teddy, Jamison, PA, UNITED STATES
Picard, Gilles J., Brussels, BELGIUM

PA Schering Corporation (U.S. corporation)

PI US 2002151536 A1 20021017

AI US 2002-57323 A1 20020125 (10)

PRAI US 2001-264396P 20010126 (60)
US 2001-323839P 20010921 (60)

DT Utility

FS APPLICATION

LREP SCHERING-PLOUGH CORPORATION, PATENT DEPARTMENT (K-6-1, 1990), 2000 GALLOPING HILL ROAD, KENILWORTH, NJ, 07033-0530

CLMN Number of Claims: 101

ECL Exemplary Claim: 1

DRWN No Drawings

LN.CNT 5004

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

SUMM . . . halting of progression of one or more conditions, for example vascular conditions, such as hyperlipidaemia (for example atherosclerosis, hypercholesterolemia or **sitosterolemia**), vascular inflammation, stroke, diabetes, obesity and/or to reduce-the level of sterol(s) (such as cholesterol) in the plasma.

SUMM . . . inhibitor(s), to prevent or treat a condition, for example a vascular condition, such as hyperlipidaemia (for example atherosclerosis, hypercholesterolemia or **sitosterolemia**), vascular inflammation, stroke, diabetes, obesity and/or reduce the level of sterol(s) (such as cholesterol) in the plasma. As used herein,. . .

SUMM . . . MEVACOR.RTM. which is available from Merck & Co.), pravastatin

(for example PRAVACHOL.RTM. which is available from Bristol Meyers Squibb), fluvastatin, **simvastatin** (for example ZOCOR.RTM. which is available from Merck & Co.), atorvastatin, cerivastatin, CI-981, rivastatin (sodium 7-(4-fluorophenyl)-2,6-diisopropyl-5-methoxymethylpyridin-3-yl)-3,5-dihydroxy-6-heptanoate), rosuvastatin, pitavastatin (such as. . . NB-598 ((E)--N-ethyl-N-(6,6-dimethyl-2-hepten-4-ynyl)-3-[(3,3'-bithiophen-5-yl)methoxy]benzene-methanamine hydrochloride) and other sterol biosynthesis inhibitors such as DMP-565. Preferred HMG CoA reductase inhibitors include lovastatin, pravastatin and **simvastatin**. The most preferred HMG CoA reductase inhibitor is **simvastatin**.

SUMM . . . Preferably the cholesterol biosynthesis inhibitor comprises one or more HMG CoA reductase inhibitors, such as, for example, lovastatin, pravastatin and/or **simvastatin**. More preferably, the composition or treatment comprises the compound of Formula (II) in combination with **simvastatin** and gemfibrozil or fenofibrate.

SUMM . . . treat one or more conditions, for example vascular conditions such as atherosclerosis, hyperlipidaemia (including but not limited to hypercholesterolemia, hypertriglyceridaemia, **sitosterolemia**), vascular inflammation, stroke, diabetes, obesity, and/or reduce the level of sterol(s) in the plasma. The compositions and treatments can be. . .

DETD . . . and can be useful in the treatment and/or prevention of conditions, for example vascular conditions, such as atherosclerosis, hypercholesterolemia and **sitosterolemia**, stroke, obesity and lowering of plasma levels of cholesterol in mammals, in particular in mammals.

CLM What is claimed is:

. . . 15, wherein the at least one HMG CoA reductase inhibitor is selected from the group consisting of lovastatin, pravastatin, fluvastatin, **simvastatin**, atorvastatin, rosuvastatin, cerivastatin and mixtures thereof.

17. The composition according to claim 16, wherein the at least one HMG CoA reductase inhibitor is **simvastatin**.

18. The composition according to claim 12, further comprising **simvastatin**.

46. The composition according to claim 45, wherein the at least one HMG CoA reductase inhibitor is **simvastatin**.

52. The method of claim 51, wherein the HMG CoA reductase inhibitor is **simvastatin**.

IT 59-67-6, Nicotinic acid, biological studies 637-07-0, Clofibrate 943-45-3D, Fibric acid, derivs. 5868-05-3, Niceritrol 11041-12-6, Cholestyramine 15351-13-0, Nicofuranose 23288-49-5, Probucol 25812-30-0, Gemfibrozil 30299-08-2, Clinofibrate 41859-67-0, Bezafibrate 49562-28-9, Fenofibrate 50925-79-6, Colestipol 51037-30-0, Acipimox 52214-84-3, Ciprofibrate 69047-39-8, Binifibrate 75330-75-5, Lovastatin **79902-63-9**, Simvastatin 81093-37-0, Pravastatin 93957-54-1, Fluvastatin 96609-16-4, Lifibrol 134523-00-5, Atorvastatin 145599-86-6, Cerivastatin
(combinations of nicotinic acid and derivs. and azetidine sterol absorption inhibitor(s) for treatment of vascular indications)

L10 ANSWER 17 OF 19 USPATFULL on STN

AB The present invention provides compositions, therapeutic combinations and methods including: (a) at least one sterol absorption inhibitor; and (b) at least one blood modifier, which can be useful for treating vascular conditions and lowering plasma levels of sterols.

AN 2002:266305 USPATFULL

TI Combinations of sterol absorption inhibitor(s) with blood modifier(s)

for treating vascular conditions
IN Kosoglou, Teddy, Jamison, PA, UNITED STATES
Ress, Rudyard J., Flemington, NJ, UNITED STATES
Strony, John T., Lebanon, NJ, UNITED STATES
Veltri, Enrico P., Princeton, NJ, UNITED STATES
PA Schering Corporation (U.S. corporation)
PI US 2002147184 A1 20021010
AI US 2002-56680 A1 20020125 (10)
PRAI US 2001-324123P 20010921 (60)
US 2001-264396P 20010126 (60)
US 2001-264600P 20010126 (60)
US 2001-264275P 20010126 (60)
DT Utility
FS APPLICATION
LREP SCHERING-PLOUGH CORPORATION, PATENT DEPARTMENT (K-6-1, 1990), 2000 GALLOPING HILL ROAD, KENILWORTH, NJ, 07033-0530
CLMN Number of Claims: 48
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 3296
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
DETD . . . in a therapeutically effective amount to treat "vascular conditions" such as atherosclerosis, hyperlipidaemia (including but not limited to hypercholesterolaemia, hypertriglyceridaemia, **sitosterolemia**), vascular inflammation, hypertension, angina, cardiac arrhythmias, stroke, as well as conditions such diabetes, obesity, and/or to reduce the level of. . .
DETD . . . MEVACOR.RTM. which is available from Merck & Co.), pravastatin (for example PRAVACHOL.RTM. which is available from Bristol Meyers Squibb), fluvastatin, **simvastatin** (for example ZOCOR.RTM. which is available from Merck & Co.), atorvastatin, cerivastatin, rosuvastatin, rivastatin (sodium 7-(4-fluorophenyl)-2,6-diisopropyl-5-methoxymethylpyridin-3-yl)-3,5-dihydroxy-6-heptanoate CI-981 and pitavastatin (such. . . NB-598 ((E)--N-ethyl-N-(6,6-dimethyl-2-hepten-4-ynyl)-3-[(3,3'-bithiophen-5-yl)methoxy]benzene-methanamine hydrochloride) and other sterol biosynthesis inhibitors such as DMP-565. Preferred HMG CoA reductase inhibitors include lovastatin, pravastatin and **simvastatin**. The most preferred HMG CoA reductase inhibitor is **simvastatin**.
DETD . . . Preferably the cholesterol biosynthesis inhibitor comprises one or more HMG CoA reductase inhibitors, such as, for example, lovastatin, pravastatin and/or **simvastatin**.
DETD . . . mammals, and can be useful in the treatment and/or prevention of vascular conditions, such as vascular inflammation, atherosclerosis, hypercholesterolemia and **sitosterolemia**, stroke, vascular conditions and lowering of plasma levels of cholesterol in mammals, in particular in humans.
CLM What is claimed is:
37. The composition according to claim 36, wherein the at least one HMG CoA reductase inhibitor is **simvastatin**.

IT 59-67-6, Nicotinic acid, biological studies 637-07-0, Clofibrate 943-45-3D, Fibric acid, derivs. 5868-05-3, Niceritrol 11041-12-6, Cholestyramine 15351-13-0, Nicofuranose 23288-49-5, Probucol 25812-30-0, Gemfibrozil 30299-08-2, Clinofibrate 41859-67-0, Bezafibrate 49562-28-9, Fenofibrate 50925-79-6, Colestipol 51037-30-0, Acipimox 52214-84-3, Ciprofibrate 69047-39-8, Binifibrate 75330-75-5, Lovastatin **79902-63-9**, Simvastatin 81093-37-0, Pravastatin 93957-54-1, Fluvastatin 96609-16-4, Lifibrol 134523-00-5, Atorvastatin 145599-86-6, Cerivastatin
(combinations of nicotinic acid and derivs. and azetidine sterol absorption inhibitor(s) for treatment of vascular indications)

L10 ANSWER 18 OF 19 CAPLUS COPYRIGHT 2003 ACS on STN DUPLICATE 3

AB The review on clin. trials establishing the efficacy and safety of ezetimibe 10 mg once daily, as monotherapy and co-administered with statins, for the treatment of hypercholesterolemia. As monotherapy, ezetimibe produced redns. in low-d. lipoprotein cholesterol (LDL-C) of approx. 18% ($P < 0.01$ compared with placebo). As add-on therapy for patients who failed to meet target redns. with statin monotherapy, the addn. of ezetimibe produced a 21.4% addnl. redn. in LDL-C compared with statin monotherapy ($P < 0.001$). Addn. of ezetimibe to statin therapy also significantly improved high-d. lipoprotein cholesterol and triglyceride levels compared with statin monotherapy ($P < 0.05$, $P < 0.001$, resp.). In four studies in which ezetimibe 10 mg was co-administered with **simvastatin**, atorvastatin, pravastatin, or lovastatin at different dosages, redns. in LDL-C levels with co-administration were significantly greater than those obtained with the corresponding statin monotherapy dose. Ezetimibe plus 10 mg of **simvastatin** or atorvastatin produced LDL-C redns. comparable to 80 mg of the resp. statin monotherapy. In all the clin. trials, ezetimibe was well tolerated, with a safety profile comparable to that of statin monotherapy and to that of placebo. Drug-drug interactions have not been obsd. when ezetimibe is given concomitantly with statins, fenofibrate, oral contraceptives, or a no. of other commonly administered drugs. In the phase II and phase III clin. trial development program, ezetimibe has been shown to be an effective and safe new option for treating hypercholesterolemia even in difficult-to-treat populations such as homozygous and heterozygous familial hypercholesterolemia and **sitosterolemia**.

AN 2003:30938 CAPLUS
DN 138:66084
TI Ezetimibe: efficacy and safety in clinical trials
AU Ballantyne, C. M.
CS Center for Cardiovascular Disease Prevention, Methodist DeBakey Heart Center, Baylor College of Medicine, TX, USA
SO European Heart Journal Supplements (2002), 4(Suppl. J), J9-J18
CODEN: EHJSFT; ISSN: 1520-765X
PB W. B. Saunders
DT Journal; General Review
LA English
RE.CNT 34 THERE ARE 34 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT
AB The review on clin. trials establishing the efficacy and safety of ezetimibe 10 mg once daily, as monotherapy and co-administered with statins, for the treatment of hypercholesterolemia. As monotherapy, ezetimibe produced redns. in low-d. lipoprotein cholesterol (LDL-C) of approx. 18% ($P < 0.01$ compared with placebo). As add-on therapy for patients who failed to meet target redns. with statin monotherapy, the addn. of ezetimibe produced a 21.4% addnl. redn. in LDL-C compared with statin monotherapy ($P < 0.001$). Addn. of ezetimibe to statin therapy also significantly improved high-d. lipoprotein cholesterol and triglyceride levels compared with statin monotherapy ($P < 0.05$, $P < 0.001$, resp.). In four studies in which ezetimibe 10 mg was co-administered with **simvastatin**, atorvastatin, pravastatin, or lovastatin at different dosages, redns. in LDL-C levels with co-administration were significantly greater than those obtained with the corresponding statin monotherapy dose. Ezetimibe plus 10 mg of **simvastatin** or atorvastatin produced LDL-C redns. comparable to 80 mg of the resp. statin monotherapy. In all the clin. trials, ezetimibe was well tolerated, with a safety profile comparable to that of statin monotherapy and to that of placebo. Drug-drug interactions have not been obsd. when ezetimibe is given concomitantly with statins, fenofibrate, oral contraceptives, or a no. of other commonly administered drugs. In the phase II and phase III clin. trial development program, ezetimibe has been shown to be an effective and safe new option for treating hypercholesterolemia even in difficult-to-treat populations such as homozygous and heterozygous familial hypercholesterolemia and **sitosterolemia**.

L10 ANSWER 19 OF 19 USPATFULL on STN

AB A method is provided for inhibiting onset of or treating phytosterolemia by administering to a patient an MTP inhibitor, alone or optionally, in combination with another cholesterol lowering drug, such as pravastatin.

AN 2000:54122 USPATFULL

TI Method of inhibiting or treating phytosterolemia with an MTP inhibitor

IN Gregg, Richard E., Pennington, NJ, United States

PA Bristol-Myers Squibb Company, Princeton, NJ, United States (U.S. corporation)

PI US 6057339 20000502

AI US 1998-5430 19980110 (9)

PRAI US 1997-35591P 19970117 (60)
US 1996-17224P 19960509 (60)
US 1996-17253P 19960510 (60)
US 1996-17254P 19960510 (60)
US 1996-28216P 19961001 (60)
US 1996-17253P 19960510 (60)
US 1996-17254P 19960510 (60)
US 1996-28216P 19961001 (60)
US 1996-17253P 19960510 (60)
US 1996-17254P 19960510 (60)
US 1996-28216P 19961001 (60)

DT Utility

FS Granted

EXNAM Primary Examiner: Jordan, Kimberly

LREP Rodney, Burton, Hermenau, Ronald S.

CLMN Number of Claims: 25

ECL Exemplary Claim: 1

DRWN No Drawings

LN.CNT 1261

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

SUMM . . . and Storage of Sterols Other than Cholesterol, Bjorkhem, I. and Boberg, K. M., pp. 2073-2099, phytosterolemia (also referred to as **sitosterolemia**) is a rare inherited sterol storage disease involving increased intestinal absorption of phytosterol or shellfish sterols and decreased fecal secretion.. . .

SUMM . . . compounds as disclosed in U.S. Pat. No. 4,231,938, pravastatin and related compounds such as disclosed in U.S. Pat. No. 4,346,227, **simvastatin** and related compounds as disclosed in U.S. Pat. Nos. 4,448,784 and 4,450,171, with pravastatin, lovastatin or **simvastatin** being preferred. Other HMG CoA reductase inhibitors which may be employed herein include, but are not limited to, fluvastatin, cerivastatin,. . .

SUMM Preferred are pravastatin, lovastatin or **simvastatin**.

SUMM . . . administration, a satisfactory result may be obtained employing an HMG CoA reductase inhibitor in dosages employed, for example, pravastatin, lovastatin, **simvastatin**, atorvastatin, fluvastatin or cerivastatin as indicated in the Physician's Desk Reference, such as in an amount within the range of. . .

CLM What is claimed is:
14. The method as defined in claim 13 wherein the HMG CoA reductase inhibitor is pravastatin, lovastatin, **simvastatin**, atorvastatin, fluvastatin or cerivastatin.

IT 50-78-2, Aspirin 51-49-0, Dextrothyroxine 59-67-6, Nicotinic acid, biological studies 65-49-6, p-Aminosalicylic acid 137-53-1, Sodium dextrothyroxine 637-07-0, Clofibrate 943-45-3D, Fibric acid, derivs. 1404-04-2, Neomycin 11041-12-6, Cholestyramine 23288-49-5, Probucol 25812-30-0, Gemfibrozil 30299-08-2, Clinofibrate 37296-80-3, Colestipol hydrochloride 41859-67-0, Bezafibrate 49562-28-9, Fenofibrate 50925-79-6, Colestipol 52214-84-3, Ciprofibrate 75330-75-5, Lovastatin **79902-63-9**, Simvastatin 81093-37-0, Pravastatin 93957-54-1, Fluvastatin 134523-00-5, Atorvastatin 145599-86-6, Cerivastatin 182431-06-7 182431-12-5, BMS 201238

202833-31-6, BMS-201038
(phytosterolemia treatment with microsomal triglyceride transfer protein inhibitor and cholesterol lowering drug)

=> s l6 and sitosterolemia
L11 56 L6 AND SITOSTEROLEMIA

=> s l11 and l10
L12 15 L11 AND L10

=> dup rem l12
PROCESSING COMPLETED FOR L12
L13 15 DUP REM L12 (0 DUPLICATES REMOVED)

=> d l13 1-15 ab bib kwic

L13 ANSWER 1 OF 15 USPATFULL on STN
AB The present invention provides therapeutic combinations and methods including at least one sterol or 5.alpha.-stanol absorption inhibitor that can be useful for treating xanthomas.
AN 2003:173961 USPATFULL
TI Methods and therapeutic combinations for the treatment of xanthoma using sterol absorption inhibitors
IN Davis, Harry R., Berkeley Heights, NJ, UNITED STATES
PA Schering Corporation (U.S. corporation)
PI US 2003119809 A1 20030626
AI US 2002-247095 A1 20020919 (10)
PRAI US 2001-323942P 20010921 (60)
DT Utility
FS APPLICATION
LREP SCHERING-PLOUGH CORPORATION, PATENT DEPARTMENT (K-6-1, 1990), 2000 GALLOPING HILL ROAD, KENILWORTH, NJ, 07033-0530
CLMN Number of Claims: 23
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 2722
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
SUMM . . . MEVACOR.RTM. which is available from Merck & Co.), pravastatin (for example PRAVACHOL.RTM. which is available from Bristol Meyers Squibb), fluvastatin, **simvastatin** (for example ZOCOR.RTM. which is available from Merck & Co.), atorvastatin, cerivastatin, CI-981, rivastatin (sodium 7-(4-fluorophenyl)-2,6-diisopropyl-5-methoxymethylpyridin-3-yl)-3,5-dihydroxy-6-heptanoate), rosuvastatin and pitavastatin. . . NB-598 ((E)-N-ethyl-N-(6,6-dimethyl-2-hepten-4-ynyl)-3-[(3,3'-bithiophen-5-yl)methoxy]benzene-methanamine hydrochloride) and other sterol biosynthesis inhibitors such as DMP-565. Preferred HMG CoA reductase inhibitors include lovastatin, pravastatin and **simvastatin**. The most preferred HMG CoA reductase inhibitor is **simvastatin**.
SUMM [0380] Non-limiting examples of suitable bile acid sequestrants include **cholestyramine** (a styrene-divinylbenzene copolymer containing quaternary ammonium cationic groups capable of binding bile acids, such as QUESTRAN.RTM. or QUESTRAN LIGHT.RTM. **cholestyramine** which are available from Bristol-Myers Squibb), colestipol (a copolymer of diethylenetriamine and 1-chloro-2,3-epoxypropane, such as COLESTID.RTM. tablets which are available. . .
DETD . . . cholesterol in mammals, and can be useful in the treatment and/or prevention of vascular conditions, such as atherosclerosis, hypercholesterolemia and **sitosterolemia**, vascular inflammation, stroke, obesity and lowering of plasma levels of cholesterol in subjects, in particular in humans. As used herein,. . .
CLM What is claimed is:
. . . The method according to claim 13, wherein the HMG-CoA reductase

inhibitor is selected from the group consisting of pravastatin, lovastatin, **simvastatin**, fluvastatin, rivastatin, rosuvastatin, atorvastatin, cerivastatin, and combinations thereof.

IT 59-67-6, Nicotinic acid, biological studies 59-67-6D, Nicotinic acid, derivs. 23288-49-5, Probucol 23288-49-5D, Probucol, derivs. 55121-56-7D, Azetidinone, derivs. 75330-75-5, Lovastatin **79902-63-9**, Simvastatin 81093-37-0, Pravastatin 93957-54-1, Fluvastatin 134523-00-5, Atorvastatin 143201-11-0, Rivastatin 145599-86-6, Cerivastatin 287714-41-4, Rosuvastatin
(sterol/5.alpha.-stanol absorption inhibitors for treatment of xanthoma, and use with other agents)

L13 ANSWER 2 OF 15 USPATFULL on STN

AB The present invention relates to methods of treating or preventing cardiovascular conditions while preventing or minimizing muscular degeneration side effects associated with certain HMG-CoA reductase inhibitors by coadministration of at least one sterol or 5.alpha.-stanol absorption inhibitor, pharmaceutically acceptable salts or solvates thereof, and at least one HMG-CoA reductase inhibitor, the latter being used sparingly in amounts insufficient to cause muscle degeneration.

AN 2003:173960 USPATFULL

TI Methods of treating or preventing cardiovascular conditions while preventing or minimizing muscular degeneration side effects

IN LeBeaut, Alexandre P., Morristown, NJ, UNITED STATES
Davis, Harry R., Berkeley Heights, NJ, UNITED STATES

PA Schering Corporation (U.S. corporation)

PI US 2003119808 A1 20030626

AI US 2002-246996 A1 20020919 (10)

PRAI US 2001-324121P 20010921 (60)
US 2002-351957P 20020125 (60)

DT Utility

FS APPLICATION

LREP SCHERING-PLOUGH CORPORATION, PATENT DEPARTMENT (K-6-1, 1990), 2000 GALLOPING HILL ROAD, KENILWORTH, NJ, 07033-0530

CLMN Number of Claims: 23

ECL Exemplary Claim: 1

DRWN No Drawings

LN.CNT 3092

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

SUMM . . . MEVACOR.RTM. which is available from Merck & Co.), pravastatin (for example PRAVACHOL.RTM. which is available from Bristol Meyers Squibb), fluvastatin, **simvastatin** (for example ZOCOR.RTM. which is available from Merck & Co.), atorvastatin, [cerivastatin] withdrawn from the market, CI-981, rivastatin (sodium 7-(4-fluorophenyl)-2,6-diisopropyl-5-methoxymethylpyridin-3-yl)-3,5-dihydroxy-6-heptanoate). . . pitavastatin (such as NK-104 of Negma Kowa of Japan). Preferred HMG CoA reductase inhibitors include lovastatin, pravastatin , atorvastatin and **simvastatin**. The most preferred HMG CoA reductase inhibitors are **simvastatin** and atorvastatin.

SUMM . . . with the at least one sterol or 5.alpha.-stanol absorption inhibitor, e.g.;

HMG CoA Reductase Inhibitor	Approved Dose (mg)
simvastatin	5, 10, 20, 40, 80
pravastatin	10, 20, 40
atorvastatin	10, 20, 40, 80
lovastatin	10, 20, 40

SUMM [0393] Non-limiting examples of suitable bile acid sequestrants include **cholestyramine** (a styrene-divinylbenzene copolymer containing quaternary ammonium cationic groups capable of binding bile acids, such

as QUESTRAN.RTM. or QUESTRAN LIGHT.RTM. **cholestyramine** which are available from Bristol-Myers Squibb), colestipol (a copolymer of diethylenetriamine and 1-chloro-2,3-epoxypropane, such as COLESTID.RTM. tablets which are available. . .

SUMM . . . can further be used to treat or prevent vascular disease or conditions (such as for example atherosclerosis, arteriosclerosis, hypercholesterolemia and/or **sitosterolemia**), cardiovascular events, hypertension, obesity, stroke, lowering of a concentration of a sterol in plasma of a mammal, reducing vascular inflammation. . .

SUMM . . . the above-described tablet can be coadministered with a tablet, capsule, etc. comprising a dosage of Active Compound II, for example **simvastatin** as described above.

SUMM . . . 5.alpha.-stanols in subjects and can be useful in the treatment and/or prevention of vascular conditions, such as atherosclerosis, hypercholesterolemia and **sitosterolemia**, stroke, obesity and lowering of plasma levels of sterols such as cholesterol or 5.alpha.-stanols in subject, in particular in humans.

CLM What is claimed is:

. . . 1, wherein the at least one HMG-CoA reductase inhibitor is selected from the group consisting of lovastatin, pravastatin, rivastatin, fluvastatin, **simvastatin**, atorvastatin, cerivastatin and combinations thereof.

15. The method of claim 1, wherein the at least one HMG-CoA reductase inhibitor is **simvastatin**.

IT 75330-75-5, Lovastatin **79902-63-9**, Simvastatin 81093-37-0, Pravastatin 93957-54-1, Fluvastatin 134523-00-5, Atorvastatin 143201-11-0, Rivastatin 145599-86-6, Cerivastatin
(HMG-CoA reductase inhibitor; sterol or 5.alpha.-stanol absorption inhibitor and HMG-CoA reductase inhibitor for treating or preventing cardiovascular conditions while preventing muscle degeneration side effects)

L13 ANSWER 3 OF 15 USPATFULL on STN

AB The present invention provides compositions, therapeutic combinations and methods including: (a) at least one hormone replacement therapy composition; and (b) at least one sterol absorption inhibitor which can be useful for treating vascular conditions in post-menopausal women and lowering plasma levels of sterols or 5.alpha.-stanols.

AN 2003:173948 USPATFULL

TI Combinations of hormone replacement therapy composition(s) and sterol absorption inhibitor(s) and treatments for vascular conditions in post-menopausal women

IN Strony, John T., Lebanon, NJ, UNITED STATES

PA Schering Corporation (U.S. corporation)

PI US 2003119796 A1 20030626

AI US 2002-247085 A1 20020919 (10)

RLI Continuation-in-part of Ser. No. US 2002-166942, filed on 11 Jun 2002, PENDING

PRAI US 2001-324118P 20010921 (60)

DT Utility

FS APPLICATION

LREP SCHERING-PLOUGH CORPORATION, PATENT DEPARTMENT (K-6-1, 1990), 2000 GALLOPING HILL ROAD, KENILWORTH, NJ, 07033-0530

CLMN Number of Claims: 44

ECL Exemplary Claim: 1

DRWN No Drawings

LN.CNT 2932

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

SUMM . . . or halting of progression of the condition, for example a vascular condition, such as hyperlipidaemia (for example atherosclerosis, hypercholesterolemia or **sitosterolemia**), vascular inflammation, stroke, diabetes, obesity and/or reduce the level

of sterol(s) (such as cholesterol) in the plasma of a patient,. . .

SUMM . . . MEVACOR.RTM. which is available from Merck & Co.), pravastatin (for example PRAVACHOL.RTM. which is available from Bristol Meyers Squibb), fluvastatin, **simvastatin** (for example ZOCOR.RTM. which is available from Merck & Co.), atorvastatin, cerivastatin, CI-981, rivastatin (sodium 7-(4-fluorophenyl)-2,6-diisopropyl-5-methoxymethylpyridin-3-yl)-3,5-dihydroxy-6-heptanoate) and pitavastatin (such as. . . NB-598 ((E)-N-ethyl-N-(6,6-dimethyl-2-hepten-4-ynyl)-3-[(3,3'-bithiophen-5-yl)methoxy]benzene-methanamine hydrochloride) and other sterol biosynthesis inhibitors such as DMP-565. Preferred HMG CoA reductase inhibitors include lovastatin, pravastatin and **simvastatin**. The most preferred HMG CoA reductase inhibitor is **simvastatin**.

SUMM [0406] Non-limiting examples of suitable bile acid sequestrants include **cholestyramine** (a styrene-divinylbenzene copolymer containing quaternary ammonium cationic groups capable of binding bile acids, such as QUESTRAN.RTM. or QUESTRAN LIGHT.RTM. **cholestyramine** which are available from Bristol-Myers Squibb), colestipol (a copolymer of diethylenetriamine and 1-chloro-2,3-epoxypropane, such as COLESTID.RTM. tablets which are available. . .

DETD . . . 5.alpha.-stanol in subjects and can be useful in the treatment and/or prevention of vascular conditions, such as atherosclerosis, hypercholesterolemia and **sitosterolemia**, stroke, obesity and lowering of plasma levels of cholesterol in mammals, in particular in humans such as women, and preferably. . .

CLM What is claimed is:

. . . 22, wherein the at least one HMG CoA reductase inhibitor is selected from the group consisting of lovastatin, pravastatin, fluvastatin, **simvastatin**, atorvastatin, cerivastatin and mixtures thereof.

24. The composition according to claim 23, wherein the at least one HMG CoA reductase inhibitor is **simvastatin**.

IT 50-28-2, Estradiol, biological studies 57-63-6, Ethinyl estradiol 57-83-0, Pregn-4-ene-3, 20-dione, biological studies 58-18-4, Methyltestosterone 59-67-6, Nicotinic acid, biological studies 68-22-4, Norethindrone 71-58-9, Medroxyprogesterone acetate 72-33-3, Mestranol 297-76-7, Ethynodiol diacetate 438-67-5, Sodium estrone sulfate 520-85-4, Medroxyprogesterone 797-63-7, Levonorgestrel 4999-79-5, 17.beta.-Estradiol sodium sulfate 6533-00-2, Norgestrel 16680-47-0, Sodium equilin sulfate 16680-48-1, Equilenin sodium sulfate 16680-49-2, Sodium 17.beta.-dihydroequilin sulfate 16680-50-5, 17.beta.-Dihydroequilenin sodium sulfate 23288-49-5, Probucol 35189-28-7, Norgestimate 38600-07-6, Sodium 17.alpha.-estradiol sulfate 38600-08-7, Sodium 17.alpha.-dihydroequilenin sulfate 38600-09-8, Sodium 17.alpha.-dihydroequilin sulfate 54024-22-5, Desogestrel 75330-75-5, Lovastatin **79902-63-9**, Simvastatin 81093-37-0, Pravastatin 93957-54-1, Fluvastatin 134523-00-5, Atorvastatin 145599-86-6, Cerivastatin
(combinations of hormone replacement therapy compn.(s) and sterol absorption inhibitor(s) and treatments for vascular conditions in post-menopausal women)

L13 ANSWER 4 OF 15 USPATFULL on STN

AB The present invention provides methods for treating or preventing vascular inflammation or for reducing blood levels of c-reactive protein by administering at least one sterol absorption inhibitor and/or at least one 5.alpha.-stanol absorption inhibitor.

AN 2003:173909 USPATFULL

TI Methods for treating or preventing vascular inflammation using sterol absorption inhibitor(s)

IN Davis, Harry R., Berkeley Heights, NJ, UNITED STATES

PA Schering Corporation (U.S. corporation)

PI US 2003119757 A1 20030626

AI US 2002-247032 A1 20020919 (10)
RLI Continuation-in-part of Ser. No. US 2002-166942, filed on 11 Jun 2002, PENDING
PRAI US 2001-323937P 20010921 (60)
DT Utility
FS APPLICATION
LREP SCHERING-PLOUGH CORPORATION, PATENT DEPARTMENT (K-6-1, 1990), 2000 GALLOPING HILL ROAD, KENILWORTH, NJ, 07033-0530
CLMN Number of Claims: 35
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 3032
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

SUMM . . . MEVACOR.RTM. which is available from Merck & Co.), pravastatin (for example PRAVACHOL.RTM. which is available from Bristol Meyers Squibb), fluvastatin, **simvastatin** (for example ZOCOR.RTM. which is available from Merck & Co.), atorvastatin, cerivastatin, CI-981 and pitavastatin (such as NK-104 of Negma. . . NB-598 ((E)-N-ethyl-N-(6,6-dimethyl-2-hepten-4-ynyl)-3-[(3,3'-bithiophen-5-yl)methoxy]benzene-methanamine hydrochloride) and other sterol biosynthesis inhibitors such as DMP-565. Preferred HMG CoA reductase inhibitors include lovastatin, pravastatin and **simvastatin**. The most preferred HMG CoA reductase inhibitor is **simvastatin**.

SUMM . . . Preferably the cholesterol biosynthesis inhibitor comprises one or more HMG CoA reductase inhibitors, such as, for example, lovastatin, pravastatin and/or **simvastatin**. More preferably, the method comprises the compound of Formula (II) in combination with **simvastatin** and gemfibrozil or fenofibrate.

SUMM [0405] Non-limiting examples of suitable bile acid sequestrants include **cholestyramine** (a styrene-divinylbenzene copolymer containing quaternary ammonium cationic groups capable of binding bile acids, such as QUESTRAN.RTM. or QUESTRAN LIGHT.RTM. **cholestyramine** which are available from Bristol-Myers Squibb), colestipol (a copolymer of diethylenetriamine and 1-chloro-2,3-epoxypropane, such as COLESTID.RTM. tablets which are available. . .

DETD . . . blood and can be useful in the treatment as well as prevention of vascular conditions, such as atherosclerosis, hypercholesterolemia and **sitosterolemia**, stroke, obesity and lower plasma levels of sterols and/or 5.alpha.-stanols in a subject, in particular in humans, such as phytosterols. . .

DETD . . . 12 consecutive weeks: a tablet formulation as described above having 10 milligrams of the compound of Formula (II) "Composition A"; **SIMVASTATIN** 10, 20, 40 or 80 mg (available from Merck & Co., Inc.); coadministration of Composition A+**SIMVASTATIN** 10, 20, 40 or 80 mg; or placebo.

DETD [0512] Pooled subjects treated with Composition A+**SIMVASTATIN** had reduced LDL-C from baseline by 49.9% vs. pooled subjects treated with **SIMVASTATIN** alone (36.1%, P<0.01) and co-administration of Composition A+**SIMVASTATIN** was superior to statin alone at each **SIMVASTATIN** dose. Overall, median percent reductions in CRP from baseline were almost 2.times.greater with pooled Composition A+**SIMVASTATIN** vs. pooled **SIMVASTATIN** alone (-34.8% vs -18.2%, P<0.01). Median CRP was reduced in pooled Composition A+**SIMVASTATIN** to 0.180 mg/dL and with **SIMVASTATIN** to 0.215 mg/dL (P=0.03). CRP reductions by Composition A+**SIMVASTATIN** were comparable to **SIMVASTATIN** 80.

CLM What is claimed is:

. . . 19, wherein the at least one HMG CoA reductase inhibitor is selected from the group consisting of lovastatin, pravastatin, fluvastatin, **simvastatin**, atorvastatin, cerivastatin and mixtures thereof.

IT 75330-75-5, Lovastatin **79902-63-9**, Simvastatin 81093-37-0, Pravastatin 93957-54-1, Fluvastatin 134523-00-5, Atorvastatin 145599-86-6, Cerivastatin

(HMG-CoA reductase inhibitor; sterol or 5.alpha.-stanol absorption inhibitor for reducing blood levels of C-reactive protein and treating or preventing vascular inflammation)

L13 ANSWER 5 OF 15 USPATFULL on STN
AB The present invention provides methods for the treatment of obesity using sterol or 5.alpha.-stanol absorption inhibitors and compositions and therapeutic combinations including sterol or 5.alpha.-stanol absorption inhibitors and at least one obesity control medication.
AN 2003:173582 USPATFULL
TI Methods and therapeutic combinations for the treatment of obesity using sterol absorption inhibitors
IN Davis, Harry R., Berkeley Heights, NJ, UNITED STATES
Ress, Rudyard J., Flemington, NJ, UNITED STATES
Strony, John T., Lebanon, NJ, UNITED STATES
Veltri, Enrico P., Princeton, NJ, UNITED STATES
PA Schering Corporation (U.S. corporation)
PI US 2003119428 A1 20030626
AI US 2002-247397 A1 20020919 (10)
RLI Continuation-in-part of Ser. No. US 2002-166942, filed on 11 Jun 2002, PENDING
PRAI US 2001-323840P 20010921 (60)
DT Utility
FS APPLICATION
LREP SCHERING-PLOUGH CORPORATION, PATENT DEPARTMENT (K-6-1, 1990), 2000 GALLOPING HILL ROAD, KENILWORTH, NJ, 07033-0530
CLMN Number of Claims: 35
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 3027
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
SUMM . . . MEVACOR.RTM. which is available from Merck & Co.), pravastatin (for example PRAVACHOL.RTM. which is available from Bristol Meyers Squibb), fluvastatin, **simvastatin** (for example ZOCOR.RTM. which is available from Merck & Co.), atorvastatin, cerivastatin, CI-981, rivastatin (sodium 7-(4-fluorophenyl)-2,6-diisopropyl-5-methoxymethylpyridin-3-yl)-3,5-dihydroxy-6-heptanoate) and pitavastatin (such as. . . . NB-598 ((E)-N-ethyl-N-(6,6-dimethyl-2-hepten-4-ynyl)-3-[(3,3'-bithiophen-5-yl)methoxy]benzene-methanamine hydrochloride) and other sterol biosynthesis inhibitors such as DMP-565. Preferred HMG CoA reductase inhibitors include lovastatin, pravastatin and **simvastatin**. The most preferred HMG CoA reductase inhibitor is **simvastatin**.
SUMM [0397] Non-limiting examples of suitable bile acid sequestrants include **cholestyramine** (a styrene-divinylbenzene copolymer containing quaternary ammonium cationic groups capable of binding bile acids, such as QUESTRAN.RTM. or QUESTRAN LIGHT.RTM. **cholestyramine** which are available from Bristol-Myers Squibb), colestipol (a copolymer of diethylenetriamine and 1-chloro-2,3-epoxypropane, such as COLESTID.RTM. tablets which are available. . .
DETD . . . subjects and can be useful in the treatment and/or prevention of vascular conditions, such as vascular inflammation, atherosclerosis, hypercholesterolemia and **sitosterolemia**, stroke, obesity and lowering of plasma levels of cholesterol in subjects, in particular in humans.

L13 ANSWER 6 OF 15 USPATFULL on STN
AB Hypocholesterolemic substituted 2-azetidinone compounds of the formula: ##STR1##

are disclosed, as well as a methods of lowering cholesterol by administering said compounds, pharmaceutical compositions containing them, and the combination of a substituted 2-azetidinone cholesterol-lowering agent and a cholesterol biosynthesis inhibitor for

the treatment and prevention of atherosclerosis.

AN 2003:153360 USPATFULL

TI Substituted 2-azetidinones useful as hypocholesterolemic agents

IN Ghosal, Anima, Edison, NJ, UNITED STATES
Zbaida, Shmuel, East Brunswick, NJ, UNITED STATES
Chowdhury, Swapan K., Warren, NJ, UNITED STATES
Iannucci, Robert M., Hampton, NJ, UNITED STATES
Feng, Wenqing, Chatham, NJ, UNITED STATES
Alton, Kevin B., Cedar Knolls, NJ, UNITED STATES
Patrick, James E., Belle Mead, NJ, UNITED STATES
Davis, Harry R., Berkeley Heights, NJ, UNITED STATES

PA Schering Corporation (U.S. corporation)

PI US 2003105028 A1 20030605

AI US 2002-166942 A1 20020611 (10)

RLI Continuation-in-part of Ser. No. US 2001-23295, filed on 17 Dec 2001, PENDING

PRAI US 2000-256875P 20001220 (60)

DT Utility

FS APPLICATION

LREP SCHERING-PLOUGH CORPORATION, PATENT DEPARTMENT (K-6-1, 1990), 2000 GALLOPING HILL ROAD, KENILWORTH, NJ, 07033-0530

CLMN Number of Claims: 36

ECL Exemplary Claim: 1

DRWN No Drawings

LN.CNT 1603

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

SUMM . . . halting of progression of one or more conditions, for example vascular conditions, such as hyperlipidaemia (for example atherosclerosis, hypercholesterolemia or **sitosterolemia**), vascular inflammation, stroke, diabetes, obesity and/or to reduce the level of sterol(s) (such as cholesterol) in the plasma. As used. . .

SUMM . . . MEVACOR.RTM. which is available from Merck & Co.), pravastatin (for example PRAVACHOL.RTM. which is available from Bristol Meyers Squibb), fluvastatin, **simvastatin** (for example ZOCOR.RTM. which is available from Merck & Co.), atorvastatin, cerivastatin, CI-981, ZD4522, rivastatin (sodium 7-(4-fluorophenyl)-2,6-diisopropyl-5-methoxymethylpyridin-3-yl)-3,5-dihydroxy-6-heptanoate), rosuvastatin, pitavastatin (such. . . hydrochloride) and other sterol biosynthesis inhibitors such as DMP-565. Preferred HMG CoA reductase inhibitors include lovastatin, pravastatin, fluvastatin, atorvastatin and **simvastatin**. The most preferred HMG CoA reductase inhibitor is **simvastatin**.

SUMM . . . invention can further comprise one or more peroxisome proliferator-activated receptor (PPAR) activators (such as fibrates), bile acid sequestrants (such as **cholestyramine**), ileal bile acid transport ("IBAT") inhibitors (such as benzothiepines) or apical sodium co-dependent bile acid transport ("ASBT") inhibitors, nicotinic acid. . .

SUMM . . . and can be useful in the treatment and/or prevention of conditions, for example vascular conditions, such as atherosclerosis, hypercholesterolemia and **sitosterolemia**, stroke, obesity and lowering of plasma levels of cholesterol in mammals, in particular in humans.

CLM What is claimed is:

. . . composition according to claim 21, wherein the cholesterol biosynthesis inhibitor is selected from the group consisting of lovastatin, pravastatin, fluvastatin, **simvastatin**, atorvastatin, L-659,699, squalestatin 1, NB-598, pitavastatin and ZD4522.

23. The pharmaceutical composition according to claim 22, wherein the cholesterol biosynthesis inhibitor is **simvastatin**.

26. The method according to claim 25, wherein the cholesterol

biosynthesis inhibitor is selected from the group consisting of lovastatin, pravastatin, fluvastatin, **simvastatin**, atorvastatin, L-659,699, squalestatin 1, NB-598, pitavastatin and ZD4522.

27. The method according to claim 26, wherein the cholesterol biosynthesis inhibitor is **simvastatin**.

31. The pharmaceutical composition according to claim 30, wherein the cholesterol biosynthesis inhibitor is selected from the group consisting of lovastatin, pravastatin, fluvastatin, **simvastatin**, atorvastatin, L-659,699, squalestatin 1, NB-598, pitavastatin and ZD4522.

32. The pharmaceutical composition according to claim 31, wherein the cholesterol biosynthesis inhibitor is **simvastatin**.

35. The method according to claim 34, wherein the cholesterol biosynthesis inhibitor is selected from the group consisting of lovastatin, pravastatin, fluvastatin, **simvastatin**, atorvastatin, L-659,699, squalestatin 1, NB-598, pitavastatin and ZD4522.

36. The method according to claim 35, wherein the cholesterol biosynthesis inhibitor is **simvastatin**.

IT 29066-42-0, L 659699 75330-75-5, Lovastatin **79902-63-9**, Simvastatin 81093-37-0, Pravastatin 93957-54-1, Fluvastatin 131060-14-5, NB-598 134523-00-5, Atorvastatin 142561-96-4, Squalestatin 1 147098-20-2, ZD4522 147511-69-1, Pitavastatin
(prepn. of azetidinone glucuronide derivs. and their use as hypocholesterolemic agents combined with a cholesterol biosynthesis inhibitor for treating diabetes, obesity, vascular conditions, and lowering plasma sterol concns.)

L13 ANSWER 7 OF 15 USPATFULL on STN
AB The present invention provides compositions, therapeutic combinations and methods including: (a) at least one sterol absorption inhibitor and (b) at least one cardiovascular agent different from the sterol absorption inhibitor, which can be useful for treating vascular conditions, obesity, diabetes and lowering plasma levels of sterols.
AN 2003:100110 USPATFULL
TI Combinations of sterol absorption inhibitor(s) with cardiovascular agent(s) for the treatment of vascular conditions
IN Kosoglou, Teddy, Jamison, PA, UNITED STATES
Ress, Rudyard J., Flemington, NJ, UNITED STATES
Strony, John T., Lebanon, NJ, UNITED STATES
Veltri, Enrico P., Princeton, NJ, UNITED STATES
Hauer, William, Warren, NJ, UNITED STATES
PA Schering Corporation (U.S. corporation)
PI US 2003069221 A1 20030410
AI US 2002-57339 A1 20020125 (10)
PRAI US 2001-323842P 20010921 (60)
US 2001-264396P 20010126 (60)
US 2001-264600P 20010126 (60)
US 2001-264275P 20010126 (60)
DT Utility
FS APPLICATION
LREP SCHERING-PLOUGH CORPORATION, PATENT DEPARTMENT (K-6-1, 1990), 2000 GALLOPING HILL ROAD, KENILWORTH, NJ, 07033-0530
CLMN Number of Claims: 49
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 3423

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

SUMM . . . in a therapeutically effective amount to treat vascular conditions such as atherosclerosis, hyperlipidaemia (including but not limited to hypercholesterolaemia, hypertriglyceridaemia, **sitosterolemia**), hypertension, vascular inflammation, angina, cardiac arrhythmias, stroke, as well as diabetes, obesity, and/or to reduce the level of sterol(s) in. . .

SUMM . . . agent(s) and sterol absorption inhibitor(s), to prevent or treat a vascular condition, such as hyperlipidaemia (for example atherosclerosis, hypercholesterolemia or **sitosterolemia**), stroke, diabetes, obesity and/or reduce the level of sterol(s) in the plasma. As used herein, "vascular" comprises cardiovascular, cerebrovascular and. . .

SUMM . . . MEVACOR.RTM. which is available from Merck & Co.), pravastatin (for example PRAVACHOL.RTM. which is available from Bristol Meyers Squibb), fluvastatin, **simvastatin** (for example ZOCOR.RTM. which is available from Merck & Co.), atorvastatin, cerivastatin, rosuvastatin, rivastatin (sodium 7-(4-fluorophenyl)-2,6-diisopropyl-5-methoxymethylpyridin-3-yl)-3,5-dihydroxy-6-heptanoate, CI-981 and pitavastatin (such. . . NB-598 ((E)--N-ethyl-N-(6,6-dimethyl-2-hepten-4-ynyl)-3-[(3,3'-bithiophen-5-yl)methoxy]benzene-methanamine hydrochloride) and other sterol biosynthesis inhibitors such as DMP-565. Preferred HMG CoA reductase inhibitors include lovastatin, pravastatin and **simvastatin**. The most preferred HMG CoA reductase inhibitor is **simvastatin**.

SUMM . . . Preferably the cholesterol biosynthesis inhibitor comprises one or more HMG CoA reductase inhibitors, such as, for example, lovastatin, pravastatin and/or **simvastatin**.

SUMM [0395] Non-limiting examples of suitable bile acid sequestrants include **cholestyramine** (a styrene-divinylbenzene copolymer containing quaternary ammonium cationic groups capable of binding bile acids, such as QUESTRAN.TM. or QUESTRAN LIGHTS.RTM. **cholestyramine** which are available from Bristol-Myers Squibb), colestipol (a copolymer of diethylenetriamine and 1-chloro-2,3-epoxypropane, such as COLESTID.RTM. tablets which are available. . .

DETD . . . below, and can be useful in the treatment and/or prevention of vascular conditions, such as vascular inflammation, atherosclerosis, hypercholesterolemia and **sitosterolemia**, stroke, obesity and lowering of plasma levels of cholesterol in mammals, in particular in humans.

CLM What is claimed is:

. . . 37. The composition according to claim 36 wherein the at least one HMG CoA reductase inhibitor comprises lovastatin, pravastatin, fluvastatin, **simvastatin**, atorvastatin, rosuvastatin, rivastatin, cerivastatin and mixtures thereof.

38. The composition according to claim 37, wherein the at least one HMG CoA reductase inhibitor comprises **simvastatin**.

IT 59-67-6, Nicotinic acid, biological studies 637-07-0, Clofibrate 943-45-3D, Fibric acid, derivs. 5868-05-3, Niceritrol **11041-12-6**, Cholestyramine 15351-13-0, Nicofuranose 23288-49-5, Probucol 25812-30-0, Gemfibrozil 30299-08-2, Clinofibrate 41859-67-0, Bezafibrate 49562-28-9, Fenofibrate 50925-79-6, Colestipol 51037-30-0, Acipimox 52214-84-3, Ciprofibrate 69047-39-8, Binifibrate 75330-75-5, Lovastatin **79902-63-9**, Simvastatin 81093-37-0, Pravastatin 93957-54-1, Fluvastatin 96609-16-4, Lifibrol 134523-00-5, Atorvastatin 145599-86-6, Cerivastatin
(combinations of nicotinic acid and derivs. and azetidine sterol absorption inhibitor(s) for treatment of vascular indications)

L13 ANSWER 8 OF 15 USPATFULL on STN

AB The present invention provides compositions, therapeutic combinations

and methods including: (a) at least one bile acid sequestrant; and (b) at least one substituted azetidinone or substituted .beta.-lactam sterol absorption inhibitor which can be useful for treating vascular conditions, diabetes, obesity and lowering plasma levels of sterols.

AN 2003:78061 USPATFULL

TI Combinations of bile acid sequestrant(s) and sterol absorption inhibitor(s) and treatments for vascular indications

IN Davis, Harry R., Berkeley Heights, NJ, UNITED STATES
Kosoglou, Teddy, Jamison, PA, UNITED STATES

PA Schering Corporation (U.S. corporation)

PI US 2003053981 A1 20030320

AI US 2002-57534 A1 20020125 (10)

PRAI US 2001-264600P 20010126 (60)
US 2001-323842P 20010921 (60)

DT Utility

FS APPLICATION

LREP SCHERING-PLOUGH CORPORATION, PATENT DEPARTMENT (K-6-1, 1990), 2000 GALLOPING HILL ROAD, KENILWORTH, NJ, 07033-0530

CLMN Number of Claims: 81

ECL Exemplary Claim: 1

DRWN No Drawings

LN.CNT 4194

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

SUMM [0006] Bile acid sequestrants, such as **cholestyramine** and colestipol, can lower intrahepatic cholesterol and promote the synthesis of apo B/E (LDL) receptors which bind LDL from plasma. . .

SUMM [0223] Non-limiting examples of suitable bile acid sequestrants include **cholestyramine** (a styrene-divinylbenzene copolymer containing quaternary ammonium cationic groups capable of binding bile acids, such as QUESTRAN.RTM. or QUESTRAN LIGHT.RTM. which. . .

SUMM . . . halting of progression of one or more conditions, for example vascular conditions, such as hyperlipidemia (for example atherosclerosis, hypercholesterolemia or **sitosterolemia**), vascular inflammation, stroke, diabetes, obesity and/or to reduce the level of sterol(s) (such as cholesterol) in the plasma.

SUMM . . . inhibitor(s), to prevent or treat a condition, for example a vascular condition, such as hyperlipidaemia (for example atherosclerosis, hypercholesterolemia or **sitosterolemia**), stroke, diabetes, obesity and/or reduce the level of sterol(s) in the plasma. As used herein, "vascular" comprises cardiovascular, cerebrovascular and. . .

SUMM . . . MEVACOR.RTM. which is available from Merck & Co.), pravastatin (for example PRAVACHOL.RTM. which is available from Bristol Meyers Squibb), fluvastatin, **simvastatin** (for example ZOCOR.RTM. which is available from Merck & Co.), atorvastatin, cerivastatin, CI-981 and pitavastatin (such as NK-104 of Negma. . . NB-598 ((E)-N-ethyl-N-(6,6-dimethyl-2-hepten-4-ynyl)-3-[(3,3'-bithiophen-5-yl)methoxy]benzene-methanamine hydrochloride) and other sterol biosynthesis inhibitors such as DMP-565. Preferred HMG CoA reductase inhibitors include lovastatin, pravastatin and **simvastatin**. The most preferred HMG CoA reductase inhibitor is **simvastatin**.

SUMM . . . acid sequestrants and one or more cholesterol biosynthesis inhibitors. In this embodiment, preferably the bile acid sequestrant is selected from **cholestyramine** and/or colestipol. Preferably the cholesterol biosynthesis inhibitor comprises one or more HMG CoA reductase inhibitors, such as, for example, lovastatin, pravastatin and/or **simvastatin**. More preferably, the composition or treatment comprises the compound of Formula (II) in combination with **simvastatin** and **cholestyramine** or colestipol.

SUMM . . . in a therapeutically effective amount to treat vascular conditions such as atherosclerosis, hyperlipidaemia (including but not limited to hypercholesterolaemia, hypertriglyceridaemia, **sitosterolemia**), stroke, diabetes, obesity, and/or reduce the level of sterol(s) in the plasma. The compositions and treatments can be

administered by. . .

DETD . . . be coadministered with a tablet, capsule, etc. comprising a dosage of Active Compound II, for example a tablet of QUESTRAN.RTM. **cholestyramine** as described above.

DETD . . . cholesterol in mammals, and can be useful in the treatment and/or prevention of vascular conditions, such as atherosclerosis, hypercholesterolemia and **sitosterolemia**, stroke, diabetes, obesity and lowering of plasma levels of cholesterol in mammals, in particular in mammals.

DETD [0653] in combination with the bile acid sequestrant **cholestyramine** would have additive efficacy. Compound XII can be prepared as shown in Example 9 of U.S. Pat. No. 5,688,787, which. . .

DETD . . . hour after they were gavaged with corn oil as a Control, compound of Formula (XII) (3 mg/kg of body weight), **cholestyramine** (1 g/kg of body weight), or the compound of Formula (XII) combined with **cholestyramine** as described in Table 1 below. Two hours later, blood and liver samples were collected from each hamster. The blood. . . of liver)

Control	4945 .+-. 644	8035 .+-. 1611
Compound XII (3 mg/kg of body weight)	1438 .+-. 455 (-71%)	3755 .+-. 923 (-53%)
Cholestyramine (1 g/kg of body weight)	836 .+-. 320 (-83%)	3300 .+-. 1252 (-60%)
Compound XII (3 mg/kg) + **Cholestyramine** (1 g/kg of body weight)	478 .+-. 101 (-90%)	1196 .+-. 247 (-85%)

DETD . . . reduced plasma and liver [.sup.14C]-cholesterol levels by 71% and 53%, respectively (see Table 1). Administration of the specified dosage of **cholestyramine** alone reduced plasma and liver [.sup.14C]-cholesterol levels by 83% and 60%, respectively. The specified combination of Compound XII and **cholestyramine** resulted in reductions in plasma and hepatic (liver) [.sup.14C]-cholesterol levels by 90% and 85%, respectively (see Table 1). These results indicate that the combination of the cholesterol absorption inhibitor, Compound XII, and the bile acid sequestrant, **cholestyramine**, may have additional effects on treating hypercholesterolemia by reducing both plasma and hepatic cholesterol levels.

CLM What is claimed is:

. . . composition according to claim 1, wherein the at least one bile acid sequestrant is selected from the group consisting of **cholestyramine**, colestipol, colesevelam hydrochloride and mixtures thereof.

3. The composition according to claim 2, wherein the at least one bile acid sequestrant comprises **cholestyramine**.

10. The composition according to claim 9, wherein the at least one HMG CoA reductase inhibitor is selected from the group consisting of lovastatin, pravastatin, fluvastatin, **simvastatin**, atorvastatin, cerivastatin and mixtures thereof.

11. The composition according to claim 10, wherein the at least one HMG CoA reductase inhibitor is **simvastatin**.

IT 59-67-6, Nicotinic acid, biological studies 637-07-0, Clofibrate 943-45-3D, Fibric acid, derivs. 5868-05-3, Niceritrol **11041-12-6**, Cholestyramine 15351-13-0, Nicofuranose 23288-49-5, Probucol 25812-30-0, Gemfibrozil 30299-08-2, Clinofibrate 41859-67-0, Bezafibrate 49562-28-9, Fenofibrate 50925-79-6, Colestipol 51037-30-0, Acipimox 52214-84-3, Ciprofibrate 69047-39-8, Binifibrate 75330-75-5, Lovastatin **79902-63-9**,

Simvastatin 81093-37-0, Pravastatin 93957-54-1, Fluvastatin 96609-16-4, Lifibrol 134523-00-5, Atorvastatin 145599-86-6, Cerivastatin
(combinations of nicotinic acid and derivs. and azetidine sterol absorption inhibitor(s) for treatment of vascular indications)

L13 ANSWER 9 OF 15 CAPLUS COPYRIGHT 2003 ACS on STN

AB The invention discloses the use of sterol absorption-inhibiting compds., pharmaceutical compns. thereof, therapeutic combinations, and their use in combination with other lipid-lowering agents to treat or prevent **sitosterolemia** and/or to lower the concn. of sterol(s) other than cholesterol in plasma or tissue of a mammal. Methods of treating or preventing vascular disease and coronary events also are provided. The methodol. and compns. of the invention use substituted azetidinone compds., e.g. I (prepn. described).

AN 2002:574926 CAPLUS
DN 137:135094

TI The use of substituted azetidinone compounds for the treatment of **sitosterolemia**

IN Davis, Harry R.
PA Schering Corporation, USA

SO PCT Int. Appl., 105 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2002058696	A2	20020801	WO 2002-US1195	20020125
WO 2002058696	A3	20030313		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, HR, HU, ID, IL, IN, IS, JP, KG, KR, KZ, LC, LK, LR, LT, LU, LV, MA, MD, MG, MK, MN, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UZ, VN, YU, ZA, ZM, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

US 2002169134	A1	20021114	US 2002-57629	20020125
PRAI US 2001-264645P	P	20010126		

OS MARPAT 137:135094

TI The use of substituted azetidinone compounds for the treatment of **sitosterolemia**

AB The invention discloses the use of sterol absorption-inhibiting compds., pharmaceutical compns. thereof, therapeutic combinations, and their use in combination with other lipid-lowering agents to treat or prevent **sitosterolemia** and/or to lower the concn. of sterol(s) other than cholesterol in plasma or tissue of a mammal. Methods of treating or preventing vascular disease and coronary events also are provided. The methodol. and compns. of the invention use substituted azetidinone compds., e.g. I (prepn. described).

ST azetidinone deriv prepn **sitosterolemia** treatment; noncholesterol sterol redn azetidinone deriv; vascular disease coronary event treatment azetidinone deriv

IT Apolipoproteins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(E, apoE knockout mouse; azetidinone derivs. for treatment of **sitosterolemia**)

IT Antiarteriosclerotics
(antiatherosclerotics; azetidinone derivs. for treatment of **sitosterolemia**)

IT Antiarteriosclerotics
Arteriosclerosis

Atherosclerosis
Blood vessel, disease
Cardiovascular agents
Cardiovascular system, disease
Drug delivery systems
Human
Hypolipemic agents
(azetidinone derivs. for treatment of **sitosterolemia**)

IT Sterols
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(azetidinone derivs. for treatment of **sitosterolemia**)

IT Sequestering agents
(bile acid; azetidinone derivs. for treatment of **sitosterolemia**)

IT Drug delivery systems
(capsules; azetidinone derivs. for treatment of **sitosterolemia**)

IT Artery, disease
(coronary; azetidinone derivs. for treatment of **sitosterolemia**)

IT Liver
(hepatic sitosterol accumulation; azetidinone derivs. for treatment of **sitosterolemia**)

IT Lipoproteins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(low-d.; azetidinone derivs. for treatment of **sitosterolemia**)

IT Lipids, biological studies
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(metabolic disorders; azetidinone derivs. for treatment of **sitosterolemia**)

IT Embryophyta
(phytosterols; azetidinone derivs. for treatment of **sitosterolemia**)

IT Natural products
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(phytosterols; azetidinone derivs. for treatment of **sitosterolemia**)

IT Drug delivery systems
(prodrugs; azetidinone derivs. for treatment of **sitosterolemia**)

IT Bile acids
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(sequestrants; azetidinone derivs. for treatment of **sitosterolemia**)

IT Sterols
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(stanols, 5.alpha.-; azetidinone derivs. for treatment of **sitosterolemia**)

IT Drug delivery systems
(tablets; azetidinone derivs. for treatment of **sitosterolemia**)

IT Biological transport
(uptake; azetidinone derivs. for treatment of **sitosterolemia**)

IT 57-88-5, Cholesterol, biological studies
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(LDL; azetidinone derivs. for treatment of **sitosterolemia**)

IT 80-97-7, Cholestanol 83-45-4, Sitostanol 83-46-5 83-48-7, Stigmasterol 474-60-2, Campestanol 474-62-4, Campesterol 23290-26-8, Avenasterol
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(azetidinone derivs. for treatment of **sitosterolemia**)

IT 163222-33-1P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES

(Uses)
(azetidinone derivs. for treatment of **sitosterolemia**)
IT **11041-12-6**, **Cholestyramine** 50925-79-6, Colestipol
75330-75-5, Lovastatin **79902-63-9**, **Simvastatin**
81093-37-0, Pravastatin 93957-54-1, Fluvastatin 134523-00-5,
Atorvastatin 147511-69-1, Itavastatin 163222-33-1D, prodrug derivs.
182815-44-7, Colesevelam hydrochloride 287714-41-4, Rosuvastatin
438576-91-1 438576-91-1D, derivs. 438576-92-2 438576-92-2D, prodrug
derivs. 444313-49-9 444313-50-2 444313-51-3 444313-53-5
444313-55-7 444313-57-9 444313-59-1 444313-60-4 444313-61-5
444313-62-6
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL
(Biological study); USES (Uses)
(azetidinone derivs. for treatment of **sitosterolemia**)
IT 9028-35-7, HMG-CoA reductase
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(inhibitors; azetidinone derivs. for treatment of
sitosterolemia)
IT 163222-32-0P 163380-15-2P 191330-56-0P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
(Reactant or reagent)
(prepn. and reaction; azetidinone derivs. for treatment of
sitosterolemia)
IT 112022-81-8 112022-83-0 133472-27-2, 4-Fluorophenylzinc chloride
RL: RCT (Reactant); RACT (Reactant or reagent)
(reaction; azetidinone derivs. for treatment of **sitosterolemia**
)

L13 ANSWER 10 OF 15 USPATFULL on STN
AB The present invention provides compositions, therapeutic combinations and methods including: (a) at least one peroxisome proliferator-activated receptor activator; and (b) at least one substituted azetidinone or substituted .beta.-lactam sterol absorption inhibitor which can be useful for treating vascular conditions, diabetes, obesity and lowering plasma levels of sterols.
AN 2002:336849 USPATFULL
TI Sterol absorption inhibitor compositions
IN Cho, Wing-Kee Philip, Princeton, NJ, UNITED STATES
Davis, Harry R., Berkeley Heights, NJ, UNITED STATES
Kosoglou, Teddy, Jamison, PA, UNITED STATES
Picard, Gilles J., Braine L'Alleud, BELGIUM
PI US 2002192203 A1 20021219
AI US 2002-136968 A1 20020501 (10)
RLI Division of Ser. No. US 2002-57323, filed on 25 Jan 2002, PENDING
PRAI US 2001-264396P 20010126 (60)
US 2001-323839P 20010921 (60)
DT Utility
FS APPLICATION
LREP SCHERING-PLOUGH CORPORATION, PATENT DEPARTMENT (K-6-1, 1990), 2000 GALLOPING HILL ROAD, KENILWORTH, NJ, 07033-0530
CLMN Number of Claims: 101
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 4987
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
SUMM . . . halting of progression of one or more conditions, for example vascular conditions, such as hyperlipidaemia (for example atherosclerosis, hypercholesterolemia or **sitosterolemia**), vascular inflammation, stroke, diabetes, obesity and/or to reduce the level of sterol(s) (such as cholesterol) in the plasma.
SUMM . . . inhibitor(s), to prevent or treat a condition, for example a vascular condition, such as hyperlipidaemia (for example atherosclerosis, hypercholesterolemia or **sitosterolemia**), vascular inflammation, stroke, diabetes, obesity and/or reduce the level

of sterol(s) (such as cholesterol) in the plasma. As used herein,. . .

SUMM . . . MEVACOR.RTM. which is available from Merck & Co.), pravastatin (for example PRAVACHOL.RTM. which is available from Bristol Meyers Squibb), fluvastatin, **simvastatin** (for example ZOCOR.RTM. which is available from Merck & Co.), atorvastatin, cerivastatin, CI-981, rivastatin (sodium 7-(4-fluorophenyl)-2,6-diisopropyl-5-methoxymethylpyridin-3-yl)-3,5-dihydroxy-6-heptanoate), rosuvastatin, pitavastatin (such as. . . NB-598 ((E)--N-ethyl-N-(6,6-dimethyl-2-hepten-4-ynyl)-3-[(3,3'-bithiophen-5-yl)methoxy]benzene-methanamine hydrochloride) and other sterol biosynthesis inhibitors such as DMP-565. Preferred HMG CoA reductase inhibitors include lovastatin, pravastatin and **simvastatin**. The most preferred HMG CoA reductase inhibitor is **simvastatin**.

SUMM . . . Preferably the cholesterol biosynthesis inhibitor comprises one or more HMG CoA reductase inhibitors, such as, for example, lovastatin, pravastatin and/or **simvastatin**. More preferably, the composition or treatment comprises the compound of Formula (II) in combination with **simvastatin** and gemfibrozil or fenofibrate.

SUMM . . . bind LDL from plasma to further reduce cholesterol levels in the blood. Non-limiting examples of suitable bile acid sequestrants include **cholestyramine** (a styrene-divinylbenzene copolymer containing quaternary ammonium cationic groups capable of binding bile acids, such as QUESTRAN.RTM. or QUESTRAN LIGHT.RTM. **cholestyramine** which are available from Bristol-Myers Squibb), colestipol (a copolymer of diethylenetriamine and 1-chloro-2,3-epoxypropane, such as COLESTID.RTM. tablets which are available. . .

SUMM . . . treat one or more conditions, for example vascular conditions such as atherosclerosis, hyperlipidaemia (including but not limited to hypercholesterolemia, hypertriglyceridaemia, **sitosterolemia**), vascular inflammation, stroke, diabetes, obesity, and/or reduce the level of sterol(s) in the plasma. The compositions and treatments can be. . .

DETD . . . and can be useful in the treatment and/or prevention of conditions, for example vascular conditions, such as atherosclerosis, hypercholesterolemia and **sitosterolemia**, stroke, obesity and lowering of plasma levels of cholesterol in mammals, in particular in mammals.

CLM What is claimed is:

. . . 15, wherein the at least one HMG CoA reductase inhibitor is selected from the group consisting of lovastatin, pravastatin, fluvastatin, **simvastatin**, atorvastatin, rosuvastatin, cerivastatin and mixtures thereof.

17. The composition according to claim 16, wherein the at least one HMG CoA reductase inhibitor is **simvastatin**.

18. The composition according to claim 12, further comprising **simvastatin**.

46. The composition according to claim 45, wherein the at least one HMG CoA reductase inhibitor is **simvastatin**.

52. The method of claim 51, wherein the HMG CoA reductase inhibitor is **simvastatin**.

IT 59-67-6, Nicotinic acid, biological studies 637-07-0, Clofibrate 943-45-3D, Fibric acid, derivs. 5868-05-3, Niceritrol **11041-12-6**, Cholestyramine 15351-13-0, Nicofuranose 23288-49-5, Probucol 25812-30-0, Gemfibrozil 30299-08-2, Clinofibrate 41859-67-0, Bezafibrate 49562-28-9, Fenofibrate 50925-79-6, Colestipol 51037-30-0, Acipimox 52214-84-3, Ciprofibrate 69047-39-8, Binifibrate 75330-75-5, Lovastatin **79902-63-9**, Simvastatin 81093-37-0, Pravastatin 93957-54-1, Fluvastatin 96609-16-4, Lifibrol 134523-00-5, Atorvastatin 145599-86-6,

Cerivastatin
(combinations of nicotinic acid and derivs. and azetidine sterol absorption inhibitor(s) for treatment of vascular indications)

L13 ANSWER 11 OF 15 USPATFULL on STN
AB The present invention provides compositions, therapeutic combinations and methods including: (a) at least one of nicotinic acid or derivatives thereof; and (b) at least one substituted azetidinone or substituted .beta.-lactam sterol absorption inhibitor which can be useful for treating vascular conditions, diabetes, obesity and lowering plasma levels of sterols.
AN 2002:323139 USPATFULL
TI Combinations of nicotinic acid and derivatives thereof and sterol absorption inhibitor(s) and treatments for vascular indications
IN Davis, Harry R., Berkeley Heights, NJ, UNITED STATES
Kosoglou, Teddy, Jamison, PA, UNITED STATES
PA Schering Corporation (U.S. corporation)
PI US 2002183305 A1 20021205
AI US 2002-57646 A1 20020125 (10)
PRAI US 2001-264275P 20010126 (60)
US 2001-323842P 20010921 (60)
DT Utility
FS APPLICATION
LREP SCHERING-PLOUGH CORPORATION, PATENT DEPARTMENT (K-6-1, 1990), 2000 GALLOPING HILL ROAD, KENILWORTH, NJ, 07033-0530
CLMN Number of Claims: 81
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 4256
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
SUMM . . . halting of progression of one or more conditions, for example vascular conditions, such as hyperlipidemia (for example atherosclerosis, hypercholesterolemia or **sitosterolemia**), vascular inflammation, stroke, diabetes, obesity and/or to reduce the level of sterol(s) (such as cholesterol) in the plasma.
SUMM . . . inhibitor(s), to prevent or treat a condition, for example a vascular condition, such as hyperlipidaemia (for example atherosclerosis, hypercholesterolemia or **sitosterolemia**), stroke, diabetes, obesity and/or reduce the level of sterol(s) in the plasma. As used herein, "vascular" comprises cardiovascular, cerebrovascular and. . .
SUMM . . . MEVACOR.RTM. which is available from Merck & Co.), pravastatin (for example PRAVACHOL.RTM. which is available from Bristol Meyers Squibb), fluvastatin, **simvastatin** (for example ZOCOR.RTM. which is available from Merck & Co.), atorvastatin, cerivastatin, CI-981, and pitavastatin (such as NK-104 of Negma. . . . NB-598 ((E)-N-ethyl-N-(6,6-dimethyl-2-hepten4-ynyl)-3-[(3,3'-bithiophen-5-yl)methoxy]benzene-methanamine hydrochloride) and other sterol biosynthesis inhibitors such as DMP-565. Preferred HMG CoA reductase inhibitors include lovastatin, pravastatin and **simvastatin**. The most preferred HMG CoA reductase inhibitor is **simvastatin**.
SUMM . . . Preferably the cholesterol biosynthesis inhibitor comprises one or more HMG CoA reductase inhibitors, such as, for example, lovastatin, pravastatin and/or **simvastatin**. More preferably, the composition or treatment comprises the compound of Formula (II) in combination with **simvastatin** and nicotinic acid or acipimox.
SUMM [0593] Non-limiting examples of suitable bile acid sequestrants include **cholestyramine** (a styrene-divinylbenzene copolymer containing quaternary ammonium cationic groups capable of binding bile acids, such as QUESTRAN.RTM. or QUESTRAN LIGHT.RTM. which. . .
SUMM . . . in a therapeutically effective amount to treat vascular conditions such as atherosclerosis, hyperlipidaemia (including but not limited to hypercholesterolaemia, hypertriglyceridaemia, **sitosterolemia**), stroke, diabetes, obesity, and/or reduce the

level of sterol(s) in the plasma. The compositions and treatments can be administered by. . .

DETD . . . cholesterol in mammals, and can be useful in the treatment and/or prevention of vascular conditions, such as atherosclerosis, hypercholesterolemia and **sitosterolemia**, diabetes, obesity and lowering of plasma levels of cholesterol in mammals, in particular in mammals.

CLM What is claimed is:

. . . 8, wherein the at least one HMG CoA reductase inhibitor is selected from the group consisting of lovastatin, pravastatin, fluvastatin, **simvastatin**, atorvastatin, cerivastatin and mixtures thereof.

10. The composition according to claim 9, wherein the at least one HMG CoA reductase inhibitor is **simvastatin**.

15. The composition according to claim 14, wherein the at least one bile acid sequestrant is selected from the group consisting of **cholestyramine** and colestipol.

IT 59-67-6, Nicotinic acid, biological studies 637-07-0, Clofibrate 943-45-3D, Fibric acid, derivs. 5868-05-3, Niceritrol **11041-12-6**, Cholestyramine 15351-13-0, Nicofuranose 23288-49-5, Probucol 25812-30-0, Gemfibrozil 30299-08-2, Clinofibrate 41859-67-0, Bezafibrate 49562-28-9, Fenofibrate 50925-79-6, Colestipol 51037-30-0, Acipimox 52214-84-3, Ciprofibrate 69047-39-8, Binifibrate 75330-75-5, Lovastatin **79902-63-9**, Simvastatin 81093-37-0, Pravastatin 93957-54-1, Fluvastatin 96609-16-4, Lifibrol 134523-00-5, Atorvastatin 145599-86-6, Cerivastatin
(combinations of nicotinic acid and derivs. and azetidine sterol absorption inhibitor(s) for treatment of vascular indications)

L13 ANSWER 12 OF 15 USPATFULL on STN

AB The present invention is directed to the use of sterol absorption inhibiting compounds, pharmaceutical compositions thereof, therapeutic combinations and their use in combination with other lipid lowering agents to treat or prevent **sitosterolemia** and/or to lower the concentration of sterol(s) other than cholesterol in plasma or tissue of a mammal. Methods of treating or preventing vascular disease and coronary events also are provided.

AN 2002:301589 USPATFULL

TI Use of substituted azetidinone compounds for the treatment of **sitosterolemia**

IN Davis, Harry R., Berkeley Heights, NJ, UNITED STATES

PA Schering Corporation (U.S. corporation)

PI US 2002169134 A1 20021114

AI US 2002-57629 A1 20020125 (10)

PRAI US 2001-264645P 20010126 (60)

DT Utility

FS APPLICATION

LREP SCHERING-PLOUGH CORPORATION, PATENT DEPARTMENT (K-6-1, 1990), 2000 GALLOPING HILL ROAD, KENILWORTH, NJ, 07033-0530

CLMN Number of Claims: 58

ECL Exemplary Claim: 1

DRWN No Drawings

LN.CNT 3321

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

TI Use of substituted azetidinone compounds for the treatment of **sitosterolemia**

AB . . . compounds, pharmaceutical compositions thereof, therapeutic combinations and their use in combination with other lipid lowering agents to treat or prevent **sitosterolemia** and/or to lower the concentration of sterol(s) other than cholesterol in plasma or tissue of a mammal. Methods of treating. . .

SUMM [0002] The present invention provides methods and pharmaceutical compositions for treating or preventing **sitosterolemia** by administering to a mammal in need of such treatment an effective amount of at least one treatment composition comprising. . .

SUMM [0003] **Sitosterolemia** is a genetic lipid storage disorder characterized by increased levels of sitosterol and other plant sterols in the plasma and other tissues due to increased non-selective intestinal absorption of sterols and decreased hepatic removal. Individuals having **sitosterolemia** can exhibit one or more of the following conditions: tendon and tuberous xanthomas, arthritis, hemolytic episodes, accelerated atherosclerosis and myocardial. . . can die at an early age due to extensive coronary atherosclerosis. See Nguyen et al., "Regulation of cholesterol biosynthesis in **sitosterolemia**: effects of lovastatin, **cholestyramine**, and dietary sterol restriction", Vol 32, Journal of Lipid Research, pp. 1941-1948, (1991), incorporated by reference herein.

SUMM [0004] **Sitosterolemia** can be treated with bile acid sequestrants (such as **cholestyramine**, colesevelam hydrochloride and colestipol), however, these compounds have a tendency to cause constipation in patients and therefore compliance with this. . .

SUMM [0006] An improved treatment for **sitosterolemia** is needed which can reduce the concentration of sterols in plasma and tissues and inhibit associated debilitating physical effects. Also,. . .

SUMM [0007] The present invention provides a method of treating or preventing **sitosterolemia**, comprising administering to a mammal in need of such treatment an effective amount of at least one sterol absorption inhibitor,. . .

SUMM [0008] In another embodiment, the present invention provides a method of treating or preventing **sitosterolemia**, comprising administering to a mammal in need of such treatment: (1) an effective amount of at least one sterol absorption. . .

SUMM [0009] In another embodiment, the present invention provides a method of treating or preventing **sitosterolemia** comprising administering to a mammal in need of such treatment: (1) an effective amount of at least one sterol absorption. . .

SUMM [0010] Other embodiments of the present invention include pharmaceutical compositions for the treatment or prevention of **sitosterolemia** comprising an effective amount of the compositions or combinations used in the methods described above in a pharmaceutically acceptable carrier.

SUMM [0017] The present invention provides methods, pharmaceutical compositions and combinations for treating or preventing **sitosterolemia** and conditions or symptoms associated with **sitosterolemia** such as are discussed above. Another aspect of the present invention provides methods, pharmaceutical compositions and combinations for reducing the. . . be useful in the treatment and/or prevention of vascular conditions or disease, such as vascular inflammation, arteriosclerosis, atherosclerosis, hypercholesterolemia and **sitosterolemia**, and cardiovascular events, stroke and/or obesity.

SUMM [0351] Non-limiting examples of suitable bile acid sequestrants include **cholestyramine** (a styrene-divinylbenzene copolymer containing quaternary ammonium cationic groups capable of binding bile acids, such as QUESTRAN.RTM. or QUESTRAN LIGHT.RTM. which. . .

SUMM . . . for use in the treatment compositions of the present invention include HMG CoA reductase inhibitors such as lovastatin, pravastatin, fluvastatin, **simvastatin**, atorvastatin, rosuvastatin and itavastatin. Preferred HMG CoA reductase inhibitors include lovastatin, atorvastatin and **simvastatin**. The most preferred HMG CoA reductase inhibitors are atorvastatin and **simvastatin**.

SUMM . . . Formula (VIII) in combination with a bile acid sequestrant. In this embodiment, preferably the bile acid sequestrant is selected from **cholestyramine**, colesevelam hydrochloride and colestipol. Preferably, the treatment composition comprises one or more bile acid

sequestrants such as, for example, **cholestyramine**, colesevelam hydrochloride and colestipol in combination with a compound of Formula (VIII) ##STR55##

SUMM . . . inhibitors. Preferably, the treatment composition comprises one or more HMG CoA reductase inhibitors such as, for example, lovastatin, atorvastatin and **simvastatin** in combination with a compound of Formula (VIII) ##STR56##

SUMM [0357] Still even more preferred, the treatment composition comprises compound of formula VIII in combination with atorvastatin and/or **simvastatin**.

SUMM . . . referred to herein as carrier materials). Because of their sterol absorption inhibitory activity, such pharmaceutical compositions possess utility in treating **sitosterolemia** and related disorders.

SUMM . . . can be administered to a mammal in need of such treatment in a pharmaceutically or therapeutically effective amount to treat **sitosterolemia** and/or reduce the level of sterol(s) in the plasma and tissues.

SUMM . . . therapeutic agents, such as sterol absorption inhibitor(s) and bile acid sequestrant(s) or other therapeutic vascular agents, to prevent or treat **sitosterolemia** and/or reduce the level of sterol(s) in the plasma and tissues. As used herein, "vascular" comprises cardiovascular, cerebrovascular and combinations. . .

SUMM . . . the intestinal absorption of sitosterol and can be useful in the treatment and/or prevention of vascular disease, arteriosclerosis, atherosclerosis and **sitosterolemia** in mammals, in particular in humans.

SUMM [0445] In another embodiment, the present invention provides a method of treating or preventing **sitosterolemia** comprising administering to a mammal in need of such treatment an effective amount of at least one sterol absorption inhibitor. . .

SUMM . . . and the second amount taken together in their totality comprise a therapeutically effective amount for the treatment or prevention of **sitosterolemia** in a mammal.

SUMM . . . be useful in the treatment and/or prevention of vascular conditions or disease, such as vascular inflammation, arteriosclerosis, atherosclerosis, hypercholesterolemia and **sitosterolemia**, and cardiovascular events, stroke and obesity.

DETD [0475] In a randomized multicenter, double-blind, placebo-controlled, 8-week trial, 37 human patients previously diagnosed with homozygous **sitosterolemia** were randomized to receive Compound VIII (n=30) or placebo (n=7):

DETD . . . T; Kwiterovich, Jr, P O, "Increased sitosterol absorption, decreased removal and expanded body pools compensate for reduced cholesterol synthesis in **sitosterolemia** with xanthomatosis", J Lipid Res, Vol. 30, pp 1319-30, (1989) and Lutjohann, D; Bjorkhem, I; Beil, U F, and von. . .

CLM What is claimed is:

1. A method of treating or preventing **sitosterolemia**, comprising administering to a mammal in need of such treatment an effective amount of at least one sterol absorption inhibitor,. . .

17. The method of claim 16, wherein the HMG-CoA reductase inhibitor is selected from the group consisting of **simvastatin**, lovastatin, pravastatin, fluvastatin, atorvastatin, rosuvastatin, itavastatin and mixtures thereof.

18. The method of claim 17, wherein the HMG-CoA reductase inhibitor is **simvastatin** or atorvastatin.

. . . The method of claim 22, wherein the HMG-CoA reductase inhibitor is selected from the group consisting of lovastatin, pravastatin, fluvastatin, **simvastatin**, atorvastatin, rosuvastatin, itavastatin and mixtures thereof.

24. A method of treating or preventing **sitosterolemia** comprising administering to a mammal in need of such treatment: (a) an effective amount of a sterol absorption inhibitor represented by Formula (VIII): ##STR90## and b) an effective amount of atorvastatin and/or **simvastatin**.

25. A pharmaceutical composition for the treatment or prevention of **sitosterolemia**, comprising an effective amount of the sterol absorption inhibitor used in the method of claim 1 in a pharmaceutically acceptable. . .
26. A pharmaceutical composition for the treatment or prevention of **sitosterolemia**, comprising an effective amount of the sterol absorption inhibitor used in the method of claim 8 in a pharmaceutically acceptable. . .
27. A pharmaceutical composition for the treatment or prevention of **sitosterolemia**, comprising an effective amount of the compound of Formula (VIII) ##STR91## in a pharmaceutically acceptable carrier.

28. A pharmaceutical composition for the treatment or prevention of **sitosterolemia**, comprising: a) an effective amount of the compound of Formula (VIII) ##STR92## and b) an effective amount of a lipid. . .

. . . composition of claim 29, wherein the HMG CoA reductase inhibitor is selected from the group consisting of lovastatin, pravastatin, fluvastatin, **simvastatin**, atorvastatin, rosuvastatin, itavastatin and mixtures thereof.

31. The composition of claim 30, wherein the HMG CoA reductase inhibitor is **simvastatin** or atorvastatin.

32. A method of treating or preventing **sitosterolemia**, comprising administering to a mammal in need of such treatment: (1) an effective amount of at least one sterol absorption. . .
33. A method of treating or preventing **sitosterolemia** comprising administering to a mammal in need of such treatment: (1) an effective amount of at least one sterol absorption. . .
42. The method of claim 41, wherein the HMG CoA reductase inhibitor is **simvastatin** or atorvastatin.

45. The method of claim 44, wherein the bile acid sequestrant is selected from the group consisting of **cholestyramine**, colesevelam hydrochloride, and colestipol.

46. A pharmaceutical composition for the treatment or prevention of **sitosterolemia**, comprising: a) an effective amount of the compound of Formula (VIII) ##STR95## and b) an effective amount of a bile. . .
47. The composition of claim 46, wherein the bile acid sequestrant is selected from the group consisting of **cholestyramine**, colesevelam hydrochloride, and colestipol.

. . . wherein the first amount and the second amount together comprise a therapeutically effective amount for the treatment or prevention of **sitosterolemia** in a mammal.

. . . wherein the first amount and the second amount together comprise a therapeutically effective amount for the treatment or prevention of **sitosterolemia** in a mammal.

IT **11041-12-6**, Cholestyramine 50925-79-6, Colestipol 75330-75-5, Lovastatin **79902-63-9**, Simvastatin 81093-37-0, Pravastatin 93957-54-1, Fluvastatin 134523-00-5, Atorvastatin 147511-69-1, Itavastatin 163222-33-1D, prodrug derivs. 182815-44-7, Colesevelam hydrochloride 287714-41-4, Rosuvastatin 438576-91-1 438576-91-1D,

derivs. 438576-92-2 438576-92-2D, prodrug derivs. 444313-49-9
444313-50-2 444313-51-3 444313-53-5 444313-55-7 444313-57-9
444313-59-1 444313-60-4 444313-61-5 444313-62-6
(azetidinone derivs. for treatment of sitosterolemia)

L13 ANSWER 13 OF 15 USPATFULL on STN
AB The present invention provides compositions, therapeutic combinations and methods including: (a) at least one peroxisome proliferator-activated receptor activator; and (b) at least one substituted azetidinone or substituted .beta.-lactam sterol absorption inhibitor which can be useful for treating vascular conditions, diabetes, obesity and lowering plasma levels of sterols.
AN 2002:273408 USPATFULL
TI Combinations of peroxisome proliferator-activated receptor (PPAR) activator(s) and sterol absorption inhibitor(s) and treatments for vascular indications
IN Davis, Harry R., Berkeley Heights, NJ, UNITED STATES
Kosoglou, Teddy, Jamison, PA, UNITED STATES
Picard, Gilles J., Brussels, BELGIUM
PA Schering Corporation (U.S. corporation)
PI US 2002151536 A1 20021017
AI US 2002-57323 A1 20020125 (10)
PRAI US 2001-264396P 20010126 (60)
US 2001-323839P 20010921 (60)
DT Utility
FS APPLICATION
LREP SCHERING-PLOUGH CORPORATION, PATENT DEPARTMENT (K-6-1, 1990), 2000 GALLOPING HILL ROAD, KENILWORTH, NJ, 07033-0530
CLMN Number of Claims: 101
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 5004
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
SUMM . . . halting of progression of one or more conditions, for example vascular conditions, such as hyperlipidaemia (for example atherosclerosis, hypercholesterolemia or **sitosterolemia**), vascular inflammation, stroke, diabetes, obesity and/or to reduce-the level of sterol(s) (such as cholesterol) in the plasma.
SUMM . . . inhibitor(s), to prevent or treat a condition, for example a vascular condition, such as hyperlipidaemia (for example atherosclerosis, hypercholesterolemia or **sitosterolemia**), vascular inflammation, stroke, diabetes, obesity and/or reduce the level of sterol(s) (such as cholesterol) in the plasma. As used herein,. . .
SUMM . . . MEVACOR.RTM. which is available from Merck & Co.), pravastatin (for example PRAVACHOL.RTM. which is available from Bristol Meyers Squibb), fluvastatin, **simvastatin** (for example ZOCOR.RTM. which is available from Merck & Co.), atorvastatin, cerivastatin, CI-981, rivastatin (sodium 7-(4-fluorophenyl)-2,6-diisopropyl-5-methoxymethylpyridin-3-yl)-3,5-dihydroxy-6-heptanoate), rosuvastatin, pitavastatin (such as. . . NB-598 ((E)--N-ethyl-N-(6,6-dimethyl-2-hepten-4-ynyl)-3-[(3,3'-bithiophen-5-yl)methoxy]benzene-methanamine hydrochloride) and other sterol biosynthesis inhibitors such as DMP-565. Preferred HMG CoA reductase inhibitors include lovastatin, pravastatin and **simvastatin**. The most preferred HMG CoA reductase inhibitor is **simvastatin**.
SUMM . . . Preferably the cholesterol biosynthesis inhibitor comprises one or more HMG CoA reductase inhibitors, such as, for example, lovastatin, pravastatin and/or **simvastatin**. More preferably, the composition or treatment comprises the compound of Formula (II) in combination with **simvastatin** and gemfibrozil or fenofibrate.
SUMM [0559] Non-limiting examples of suitable bile acid sequestrants include **cholestyramine** (a styrene-divinylbenzene copolymer containing quaternary ammonium cationic groups capable of binding bile acids, such as QUESTRAN.RTM. or QUESTRAN LIGHT.RTM. **cholestyramine** which

are available from Bristol-Myers Squibb), colestipol (a copolymer of diethylenetriamine and 1-chloro-2,3-epoxypropane, such as COLESTID.RTM. tablets which are available. . .

SUMM . . . treat one or more conditions, for example vascular conditions such as atherosclerosis, hyperlipidaemia (including but not limited to hypercholesterolemia, hypertriglyceridaemia, **sitosterolemia**), vascular inflammation, stroke, diabetes, obesity, and/or reduce the level of sterol(s) in the plasma. The compositions and treatments can be. . .

DETD . . . and can be useful in the treatment and/or prevention of conditions, for example vascular conditions, such as atherosclerosis, hypercholesterolemia and **sitosterolemia**, stroke, obesity and lowering of plasma levels of cholesterol in mammals, in particular in mammals.

CLM What is claimed is:

. . . 15, wherein the at least one HMG CoA reductase inhibitor is selected from the group consisting of lovastatin, pravastatin, fluvastatin, **simvastatin**, atorvastatin, rosuvastatin, cerivastatin and mixtures thereof.

17. The composition according to claim 16, wherein the at least one HMG CoA reductase inhibitor is **simvastatin**.

18. The composition according to claim 12, further comprising **simvastatin**.

46. The composition according to claim 45, wherein the at least one HMG CoA reductase inhibitor is **simvastatin**.

52. The method of claim 51, wherein the HMG CoA reductase inhibitor is **simvastatin**.

IT 59-67-6, Nicotinic acid, biological studies 637-07-0, Clofibrate 943-45-3D, Fibric acid, derivs. 5868-05-3, Niceritrol **11041-12-6**, Cholestyramine 15351-13-0, Nicofuranose 23288-49-5, Probucol 25812-30-0, Gemfibrozil 30299-08-2, Clinofibrate 41859-67-0, Bezafibrate 49562-28-9, Fenofibrate 50925-79-6, Colestipol 51037-30-0, Acipimox 52214-84-3, Ciprofibrate 69047-39-8, Binifibrate 75330-75-5, Lovastatin **79902-63-9**, Simvastatin 81093-37-0, Pravastatin 93957-54-1, Fluvastatin 96609-16-4, Lifibrol 134523-00-5, Atorvastatin 145599-86-6, Cerivastatin
(combinations of nicotinic acid and derivs. and azetidine sterol absorption inhibitor(s) for treatment of vascular indications)

L13 ANSWER 14 OF 15 USPATFULL on STN

AB The present invention provides compositions, therapeutic combinations and methods including: (a) at least one sterol absorption inhibitor; and (b) at least one blood modifier, which can be useful for treating vascular conditions and lowering plasma levels of sterols.

AN 2002:266305 USPATFULL

TI Combinations of sterol absorption inhibitor(s) with blood modifier(s) for treating vascular conditions

IN Kosoglou, Teddy, Jamison, PA, UNITED STATES
Ress, Rudyard J., Flemington, NJ, UNITED STATES
Strony, John T., Lebanon, NJ, UNITED STATES
Veltri, Enrico P., Princeton, NJ, UNITED STATES

PA Schering Corporation (U.S. corporation)

PI US 2002147184 A1 20021010

AI US 2002-56680 A1 20020125 (10)

PRAI US 2001-324123P 20010921 (60)
US 2001-264396P 20010126 (60)
US 2001-264600P 20010126 (60)
US 2001-264275P 20010126 (60)

DT Utility
FS APPLICATION
LREP SCHERING-PLOUGH CORPORATION, PATENT DEPARTMENT (K-6-1, 1990), 2000 GALLOPING HILL ROAD, KENILWORTH, NJ, 07033-0530
CLMN Number of Claims: 48
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 3296
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
DETD . . . in a therapeutically effective amount to treat "vascular conditions" such as atherosclerosis, hyperlipidaemia (including but not limited to hypercholesterolaemia, hypertriglyceridaemia, **sitosterolemia**), vascular inflammation, hypertension, angina, cardiac arrhythmias, stroke, as well as conditions such diabetes, obesity, and/or to reduce the level of. . .
DETD . . . MEVACOR.RTM. which is available from Merck & Co.), pravastatin (for example PRAVACHOL.RTM. which is available from Bristol Meyers Squibb), fluvastatin, **simvastatin** (for example ZOCOR.RTM. which is available from Merck & Co.), atorvastatin, cerivastatin, rosuvastatin, rivastatin (sodium 7-(4-fluorophenyl)-2,6-diisopropyl-5-methoxymethylpyridin-3-yl)-3,5-dihydroxy-6-heptanoate CI-981 and pitavastatin (such. . . NB-598 ((E)--N-ethyl-N-(6,6-dimethyl-2-hepten-4-ynyl)-3-[(3,3'-bithiophen-5-yl)methoxy]benzene-methanamine hydrochloride) and other sterol biosynthesis inhibitors such as DMP-565. Preferred HMG CoA reductase inhibitors include lovastatin, pravastatin and **simvastatin**. The most preferred HMG CoA reductase inhibitor is **simvastatin**.
DETD . . . Preferably the cholesterol biosynthesis inhibitor comprises one or more HMG CoA reductase inhibitors, such as, for example, lovastatin, pravastatin and/or **simvastatin**.
DETD [0404] Non-limiting examples of suitable bile acid sequestrants include **cholestyramine** (a styrene-divinylbenzene copolymer containing quaternary ammonium cationic groups capable of binding bile acids, such as QUESTRAN.RTM. or QUESTRAN LIGHT.RTM. **cholestyramine** which are available from Bristol-Myers Squibb), colestipol (a copolymer of diethylenetriamine and 1-chloro-2,3-epoxypropane, such as COLESTID.RTM. tablets which are available. . .
DETD . . . mammals, and can be useful in the treatment and/or prevention of vascular conditions, such as vascular inflammation, atherosclerosis, hypercholesterolemia and **sitosterolemia**, stroke, vascular conditions and lowering of plasma levels of cholesterol in mammals, in particular in humans.
CLM What is claimed is:
37. The composition according to claim 36, wherein the at least one HMG CoA reductase inhibitor is **simvastatin**.

IT 59-67-6, Nicotinic acid, biological studies 637-07-0, Clofibrate 943-45-3D, Fibric acid, derivs. 5868-05-3, Niceritrol **11041-12-6**, Cholestyramine 15351-13-0, Nicofuranose 23288-49-5, Probucol 25812-30-0, Gemfibrozil 30299-08-2, Clinofibrate 41859-67-0, Bezafibrate 49562-28-9, Fenofibrate 50925-79-6, Colestipol 51037-30-0, Acipimox 52214-84-3, Ciprofibrate 69047-39-8, Binifibrate 75330-75-5, Lovastatin **79902-63-9**, Simvastatin 81093-37-0, Pravastatin 93957-54-1, Fluvastatin 96609-16-4, Lifibrol 134523-00-5, Atorvastatin 145599-86-6, Cerivastatin
(combinations of nicotinic acid and derivs. and azetidine sterol absorption inhibitor(s) for treatment of vascular indications)

L13 ANSWER 15 OF 15 USPATFULL on STN
AB A method is provided for inhibiting onset of or treating phytosterolemia by administering to a patient an MTP inhibitor, alone or optionally, in combination with another cholesterol lowering drug, such as pravastatin.
AN 2000:54122 USPATFULL

TI Method of inhibiting or treating phytosterolemia with an MTP inhibitor
IN Gregg, Richard E., Pennington, NJ, United States
PA Bristol-Myers Squibb Company, Princeton, NJ, United States (U.S. corporation)
PI US 6057339 20000502
AI US 1998-5430 19980110 (9)
PRAI US 1997-35591P 19970117 (60)
US 1996-17224P 19960509 (60)
US 1996-17253P 19960510 (60)
US 1996-17254P 19960510 (60)
US 1996-28216P 19961001 (60)
US 1996-17253P 19960510 (60)
US 1996-17254P 19960510 (60)
US 1996-28216P 19961001 (60)
US 1996-17253P 19960510 (60)
US 1996-17254P 19960510 (60)
US 1996-28216P 19961001 (60)
DT Utility
FS Granted
EXNAM Primary Examiner: Jordan, Kimberly
LREP Rodney, Burton, Hermenau, Ronald S.
CLMN Number of Claims: 25
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 1261
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
SUMM . . . and Storage of Sterols Other than Cholesterol, Bjorkhem, I. and Boberg, K. M., pp. 2073-2099, phytosterolemia (also referred to as **sitosterolemia**) is a rare inherited sterol storage disease involving increased intestinal absorption of phytosterol or shellfish sterols and decreased fecal secretion.. . .
SUMM . . . compounds as disclosed in U.S. Pat. No. 4,231,938, pravastatin and related compounds such as disclosed in U.S. Pat. No. 4,346,227, **simvastatin** and related compounds as disclosed in U.S. Pat. Nos. 4,448,784 and 4,450,171, with pravastatin, lovastatin or **simvastatin** being preferred. Other HMG CoA reductase inhibitors which may be employed herein include, but are not limited to, fluvastatin, cerivastatin,. . .
SUMM Preferred are pravastatin, lovastatin or **simvastatin**.
SUMM . . . and related compounds as disclosed in U.S. Pat. No. 3,674,836, probucol and gemfibrozil being preferred, bile acid sequestrants such as **cholestyramine**, colestipol and DEAE-Sephadex (Secholex.RTM., Polidexide.RTM.), as well as clofibrate, lipostabil (Rhone-Poulenc), Eisai E-5050 (an N-substituted ethanolamine derivative), imanixil (HOE-402), tetrahydrolipstatin. . .
SUMM . . . administration, a satisfactory result may be obtained employing an HMG CoA reductase inhibitor in dosages employed, for example, pravastatin, lovastatin, **simvastatin**, atorvastatin, fluvastatin or cerivastatin as indicated in the Physician's Desk Reference, such as in an amount within the range of. . .
CLM What is claimed is:
14. The method as defined in claim 13 wherein the HMG CoA reductase inhibitor is pravastatin, lovastatin, **simvastatin**, atorvastatin, fluvastatin or cerivastatin.

. . . derivative which is gemfibrozil, fenofibrate, clofibrate, bezafibrate, ciprofibrate, clinofibrate, probucol, gemfibrozil, dextrothyroxine or its sodium salt, colestipol or its hydrochloride, **cholestyramine**, nicotinic acid, neomycin, p-aminosalicylic acid or aspirin.

IT 50-78-2, Aspirin 51-49-0, Dextrothyroxine 59-67-6, Nicotinic acid, biological studies 65-49-6, p-Aminosalicylic acid 137-53-1, Sodium dextrothyroxine 637-07-0, Clofibrate 943-45-3D, Fibric acid, derivs.

1404-04-2, Neomycin **11041-12-6**, Cholestyramine 23288-49-5, Probucol 25812-30-0, Gemfibrozil 30299-08-2, Clinofibrate 37296-80-3, Colestipol hydrochloride 41859-67-0, Bezafibrate 49562-28-9, Fenofibrate 50925-79-6, Colestipol 52214-84-3, Ciprofibrate 75330-75-5, Lovastatin **79902-63-9**, Simvastatin 81093-37-0, Pravastatin 93957-54-1, Fluvastatin 134523-00-5, Atorvastatin 145599-86-6, Cerivastatin 182431-06-7 182431-12-5, BMS 201238 202833-31-6, BMS-201038
(phytosterolemia treatment with microsomal triglyceride transfer protein inhibitor and cholesterol lowering drug)

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